PREPARATION OF GLASSES FOR *IN SITU* RADIOTHERAPY OF CANCER BY P^+ ION IMPLANTATION

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CONTENTS

GENERAL INTRODUCTION

An organ diseased with a cancer is generally excised by the surgery. Once it is excised, however, its functions can not be recovered. If only the cancer is destroyed *in situ* by some treatment without being excised, the diseased organ can recover its functions. Such treatments as chemotherapy, immunotherapy, radiotherapy and hyperthermia are useful for this purpose. None of them, however, have succeeded in giving the fatal damage to the cancer without giving side effects to the surrounding normal tissues.

In the case of radiotherapy, irradiation is generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it was recently shown that microspheres of 20 to 30 μm in diameter of some glasses are useful for *in situ* irradiation of cancers [1-4]. A glass of the composition $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) is a typical example of them. Yttrium-89 (100% natural abundance) in this glass is activated to a β-emitter ^{90}Y with a half-life of 64.1 h [5] by neutron bombardment. Although ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) are also activated to β-emitters, the half-lives of the activated ^{28}Al and ^{31}Si are only 2.52 min. and 2.62 h [5], respectively. Other silicons and oxygen are not activated by the neutron bombardment.

The β-ray penetrates only a short range about 1 cm in the living tissue. Microspheres in the given sizes are entrapped in the capillary bed of the tumors, when they are injected into the tumors through blood vessels. Therefore, the microspheres of this glass can give large local radiation dose of the short-ranged highly ionizing β-ray to the tumors with little radiation to neighboring healthy tissues, when they are injected into the tumor after activated. The radioactivity of the glass decays down to the negligible level only in 21 days [6]. This glass shows no premature or unwanted release of radioactive elements into the body, because it has a high chemical durability. This glass microsphere has been subjected to clinical trials of the irradiation of diseased kidneys and malignant tumors in the liver, radiation synovectomy of arthritic joints in Europe and U. S. A. [6-16]. It is already in commercial use in Canada since 1991 [6].

The radioactivity of this glass, however, may result in the substantial decay even before the cancer treatment because of the short half-life of 64.1 h of ^{90}Y [5]. Phosphorus-31 also shows 100% natural abundance and can be activated to a β-emitter ^{32}P with a little longer half-life of 14.3 days [5] by the neutron bombardment. The biological effectiveness of ^{32}P is estimated at about four times that of ^{90}Y. Therefore, phosphorus-containing glass is more useful for *in situ* radiotherapy than yttrium-containing glass. Glasses containing large amount of the phosphorus, however, generally show low chemical durabilities, when they are prepared by the conventional melt-quenching technique [17].

On the other hand, it has been shown in the field of semiconductors that an ion implantation technique is very useful for in controlling properties of materials. In this technique, large amount of ions exceeding the thermodynamical equilibrium limit can be introduced to the various materials [18-21], and the implanted ions can be localized at controlled depth from the surface of the host material by changing implantation energy [18-21]. Therefore, a chemically durable glass containing a large amount of the phosphorus, which is useful for *in situ* radiotherapy of cancer, is expected to be obtained by the ion implantation technique.

It is well known that a pure silica (SiO_2) glass has a high chemical durability [22-24]. Microspheres in various diameters of the silica glass are commercially available. As described above, ^{30}Si in this glass is activated to a β-emitter with only a short half-life less than 3 h, and other silicons and oxygen are not activated by the neutron bombardment [6]. Therefore, the silica glass can be a good host as well as the Y_2O_3-Al_2O_3-SiO_2 glass for the ion implantation of the phosphorus.

Ion implantation of the phosphorus into glasses was first attempted by Hosono *et al.* for a pure silica glass with doses of 3×10^{15} to 5×10^{17} cm^{-2} at 180 keV. They reported that a Si-O-Si bridging angle between SiO_4 tetrahedra is decreased by the ion implantation [25] and that the implanted phosphorus takes a form of colloidal particles 2 to 4 nm in diameter of amorphous red phosphorus [26-28]. The decrease in Si-O-Si bridging angle by the ion implantation was also reported also by Devine [29].

Later, Tagami *et al.* reported that the phosphorus takes a form of a phosphorus oxide when the phosphorus and subsequently oxygen are implanted into a silica glass [30]. Effects of ion implantation on chemical durabilities of glasses, however, have not been investigated.

The general purpose of this studies in this thesis is to reveal the fundamental conditions for obtaining a glasses for *in situ* radiotherapy by the phosphorus ion implantation. First, changes in surface structure and chemical durability with the phosphorus ion implantation were investigated for a pure silica glass plates as a function of energy of the ion implantation and dose of the implanted ion. The chemical durability of the ion-implanted silica glass plates was discussed in terms of its surface structure. On the basis of these results, the phosphorus ion implantation was applied to pure silica glass microspheres useful for actual radiotherapy. Furthermore, the phosphorus ion implantation was extended to the Y_2O_3-Al_2O_3-SiO_2 glass plates, in order to enhance their radiotherapeutic effect. The contents of respective chapters are summarized as follows.

In Chapter 1, P^+ ion implantation into silica glass plates was attempted at the acceleration energy of 20 keV with various doses. The chemical durabilities of the P^+-implanted silica glasses were examined by soaking the glasses into a hot water. The results were discussed in terms of the surface structural change by the ion implantation.

In Chapter 2, P^+ ion implantation into silica glass plates was carried out at the acceleration energy of 50 keV, which is higher than 20 keV, with

various doses. The chemical durability of the P^+-implanted glasses in relation to their surface structural change due to the ion implantation were compared with those of 20 keV implantation in Chapter 1.

In Chapter 3, acceleration energy of P^+ ion implantation into silica glass plates was increased up to 100 keV. The chemical durability of the P^+-implanted glasses in relation to their surface structural change due to the ion implantation were compared with those of 20 and 50 keV implantation in Chapters 1 and 2.

In Chapter 4, acceleration energy of P^+ ion implantation was furthermore elevated up to 200 keV, which is the highest energy available with the popular ion implanter commercialized. The chemical durability of the P^+-implanted glasses in relation to their surface structural change due to the ion implantation were compared with those of 20, 50 and 100 keV implantation in Chapters 1, 2 and 3 and the effect of implantation energy on the surface structure and chemical durability of P^+-implanted silica glass plates were discussed in this Chapter.

In Chapter 5, P^+ ion implantation was applied to silica glass microspheres 20 to 30 μm in diameter at 50 keV with different doses in order to obtain the guideline for preparing glass microspheres useful for practical *in situ* radiotherapy. The surface structural change and chemical durability of the glass microsphere were investigated in comparison with those of P^+-implanted silica glass plates described in the previous chapters. Based on these results, the method adequate for phosphorus ion

implantation into glass microspheres was discussed.

In Chapter 6, on the basis of the results on P^+ ion implantation into silica glass plates, P^+ ion implantation was extended to Y_2O_3-Al_2O_3-SiO_2 glass plates, which is already in clinical use, at 200 keV with various doses, in order to enhance the radiotherapeutic effect of the glass. The surface structure and chemical durability of the glass was also compared with those of 200 keV implantation into silica glass plates in Chapter 4 and the enhancement in radiotherapeutic effect by the P^+ ion implantation into Y_2O_3-Al_2O_3-SiO_2 glass was discussed.

In General Summary, the contents of the above Chapters are summarized with the general conclusion of the present thesis and future perspectives.

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CHAPTER 1

STRUCTURE AND PROPERTIES OF SILICA GLASS PLATES IMPLANTED WITH P^+ IONS AT 20 keV

1. Introduction

Radiotherapy is one of the effective treatments of cancer without excising its host organ. Irradiation is, however, generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it is recently reported that a glass microsphere of 20 to 30 μm in diameter of $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition is useful for *in situ* irradiation of cancers [1-4]. Yttrium-89 (100% natural abundance) in this glass is activated a β-emitter with a half-life of 64.1 h by neutron bombardment. Although ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) are also activated to β-emitters, the half-lives of the activated ^{28}Al and ^{31}Si are only 2.52 min. and 2.62 h, respectively [5]. Other silicons and oxygen are not activated by the neutron bombardment. As shown in Figure 1, when microspheres in the given sizes are injected into the tumors through blood vessels, they can give large local radiation

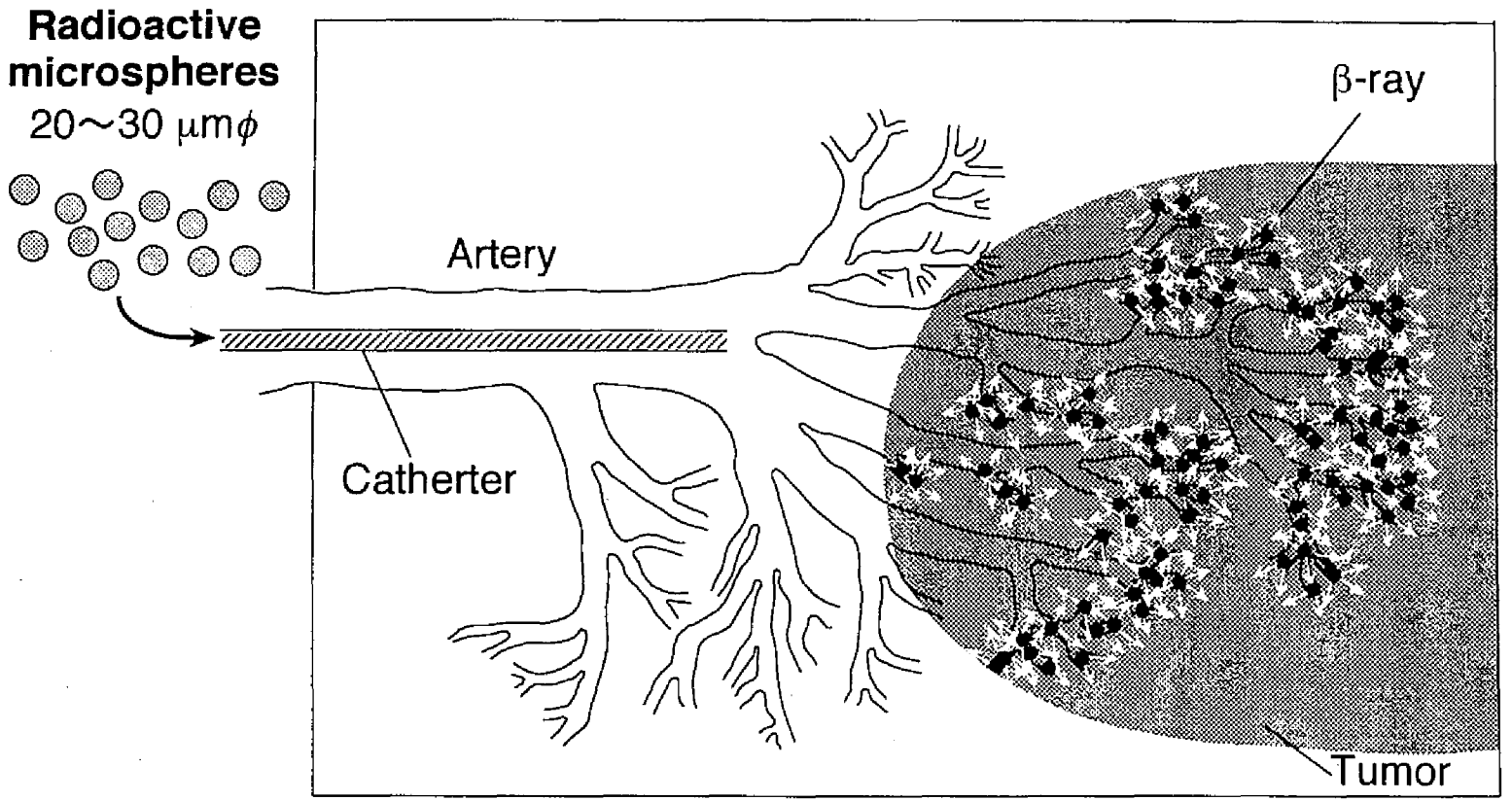

Figure 1. Cancer treatment with radioactive microspheres.

Table 1. Isotopes of phosphorus and yttrium

Nuclide	Natural abundance /%	Half-life	Radiation
^{31}P	100		
^{32}P		14.3 days	β-ray
^{89}Y	100		
^{90}Y		64.1 h	β-ray

dose of the short-ranged highly ionizing β-ray to the tumors with little radiation to neighboring healthy tissues.

The radioactivity of this glass, however, may result in the substantial decay even before the cancer treatment because of the short half-life of 64.1 h of ^{90}Y [5]. As shown in Table 1, phosphorus-31 also shows 100% natural abundance and can be activated to β-emitter ^{32}P with a little longer half-life of 14.3 days [5] by neutron bombardment. The biological effectiveness of ^{32}P is estimated at about five times that of ^{90}Y. Therefore, phosphorus-containing glass is more useful for *in situ* radiotherapy of cancer than yttrium-containing glass. Glasses containing a large amount of the phosphorus, however, generally show low chemical durabilities [6].

On the other hand, in an ion implantation technique, large amount of ions exceeding the thermodynamical equilibrium limit can be introduced to various materials and the implanted ions can be localized at controlled depth from the surface of the host material by changing implantation energy [7-10]. Consequently, ion implantation of the phosphorus into a chemically durable glass is expected to give microspheres useful for *in situ* radiotherapy of cancer.

A pure silica glass is well known to have a high chemical durability [11-13]. Microspheres with controlled diameters of a pure silica glass are commercially available. As mentioned above, ^{30}Si in this glass is activated to β-emitter with only a half-life of 2.62 h, and other silicons and oxygen are not activated by the neutron bombardment. Therefore, the

silica glass can be a good host for the ion implantation of the phosphorus.

In this chapter, the phosphorus ion was implanted into plates of highly pure silica glass at the acceleration energy of 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2}, in order to investigate fundamentally the effect of the ion implantation on the chemical durability of the silica glass. The states and distribution of the implanted phosphorus and structural change of thus implanted glass plates were examined, and chemical durabilities of the silica glass plates implanted with P^+ ions were examined by soaking the glass plates in hot water. The results were discussed in terms of their structure.

2. Experimental

2.1. P^+ Ion Implantation into Silica Glass Plates

Highly pure silica glass (metallic impurities < 0.5 ppm, OH < 100 ppm) prepared by vapor-phase axial deposition (SUMIQUARTZ SK-1300, Sumitomo Metal Industries Ltd., Tokyo, Japan) was cut into rectangular specimens 10 mm×10 mm×1 mm in size, polished with diamond paste and heated up to 1100°C at a rate of 5°C·min^{-1} and kept at given temperature for 1 h in a SiC electric furnace in order to eliminate the strains. Figure 2 shows the schematic representation of phosphorus ion implantation into a silica glass. The phosphorus ions were generated by thermoelectron

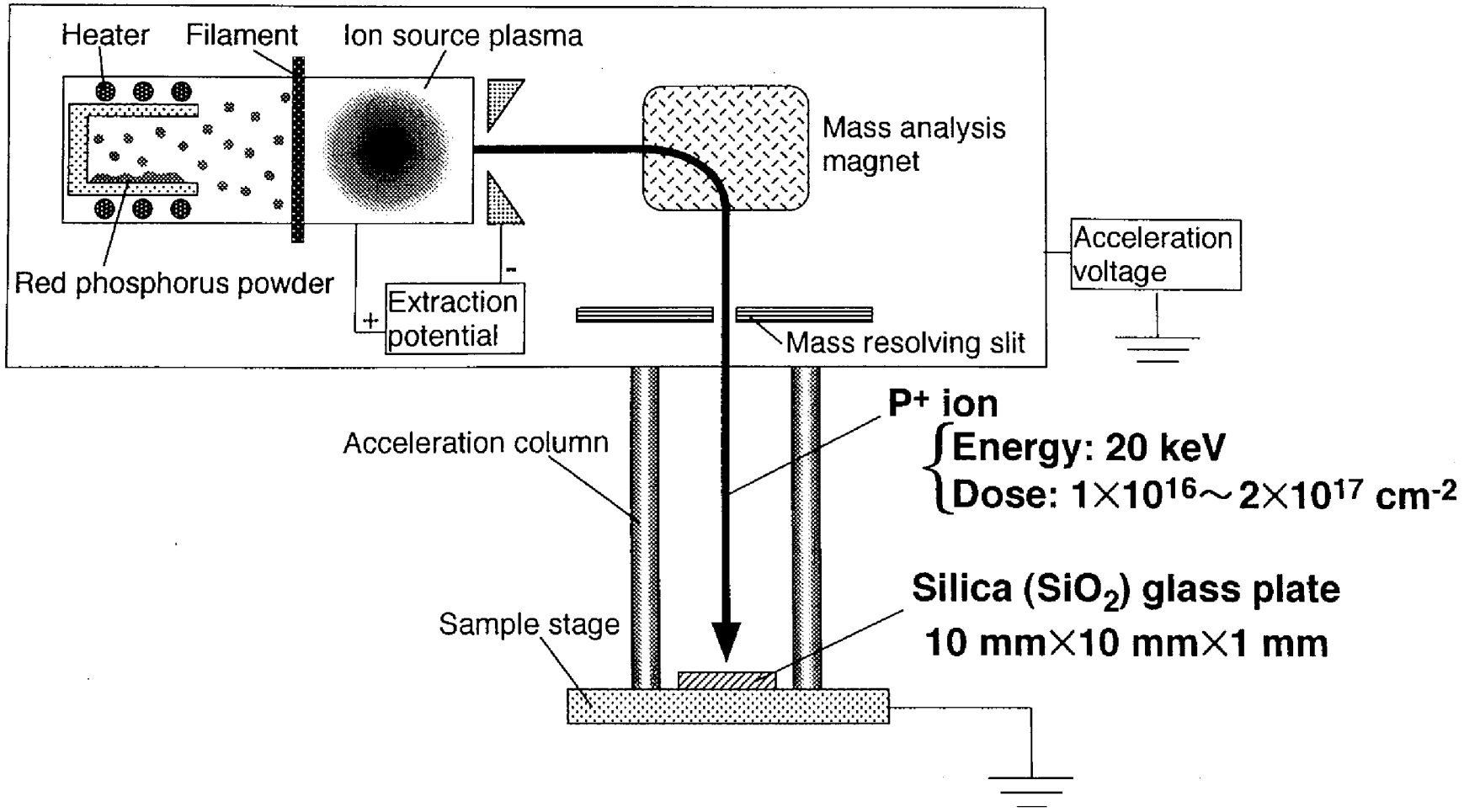

Figure 2. P^+ ion implantation into silica glass plates.

bombardment to red phosphorus vapor produced by heating red phosphorus powder. Thus obtained P^+ ions were implanted into the glass plate at 20 keV with doses of 1×10^{16}, 5×10^{16}, 1×10^{17} and 2×10^{17} cm^{-2}. It is estimated theoretically that P^+ ions, which were implanted at 20 keV, show Gaussian distribution giving the maximum concentrations at the depth of 19.9 nm from the surface of the silica glass [14]. After the ion implantation, every sample was preserved in a nitrogen atmosphere in order to prevent the oxidation of phosphorus.

2.2. Analysis of Glass Surface

The distributions of phosphorus in these glass plates were analyzed by a Rutherford backscattering spectrometry (RBS) with ion beam analyzer at Radiation Laboratory of Nuclear Engineering, Kyoto University, using 2 MeV $^4He^+$ ions with 170° incident angle. The states of phosphorus were investigated by measuring P_{2p} binding energy with an X-ray photoelectron spectroscope (XPS) (MT-5500, ULVAC-phi Co. Ltd., Chigasaki, Japan) using MgKα (1253.6 eV) X-ray as an excitation source in the 10^{-9} Pa residual pressure range. The photoelectron take-off angle (the angle between the sample surface and the detector axis) was set at 45°. Xenon-ion sputtering was carried out at 4 keV to measure the depth profiles. The sputtered depth was determined by referring the sputtering rate, 0.12 $nm\cdot min^{-1}$, of a SiO_2 film 0.35 nm thick formed on a silicon wafer. Measured binding energies were corrected by referring the binding energy

of C_{1s} of the hydrocarbon (284.6 eV) adsorbed on the glass surfaces. Surface structures of the glasses were analyzed by a Fourier transform infrared (FT-IR) reflection spectrometer (SR-5M, Japan Spectroscopic Co. Ltd., Tokyo, Japan) with 30° incident angle.

2.3. Chemical Durability Test

As shown in Figure 3, the P^+-implanted glass plates were immersed in 20 ml of distilled water at 95°C for 7 days in a polypropylene bottle, shaken at a rate of 120 strokes·min^{-1} with a stroke length of 3 cm. The concentrations of phosphorus and silicon released from the glass plates were measured by an inductively coupled plasma (ICP) atomic emission spectrometer (SPS-1500 VR, Seiko Instruments Inc., Tokyo, Japan).

3. Results

Figure 4 shows the RBS spectra of silica glasses implanted with P^+ ions at 20 keV with doses of 1×10^{16}, 5×10^{16}, 1×10^{17} and 2×10^{17} cm^{-2}. The area of the peak assigned to phosphorus increased with increasing dose up to 5×10^{16} cm^{-2}, but became almost constant for doses above 5×10^{16} cm^{-2}.

Figure 5 shows the FT-IR reflection spectrum of silica glass implanted with P^+ ions at 20 keV with a dose of 5×10^{16} cm^{-2}, in comparison with that of the unimplanted original silica glass. The silica glass

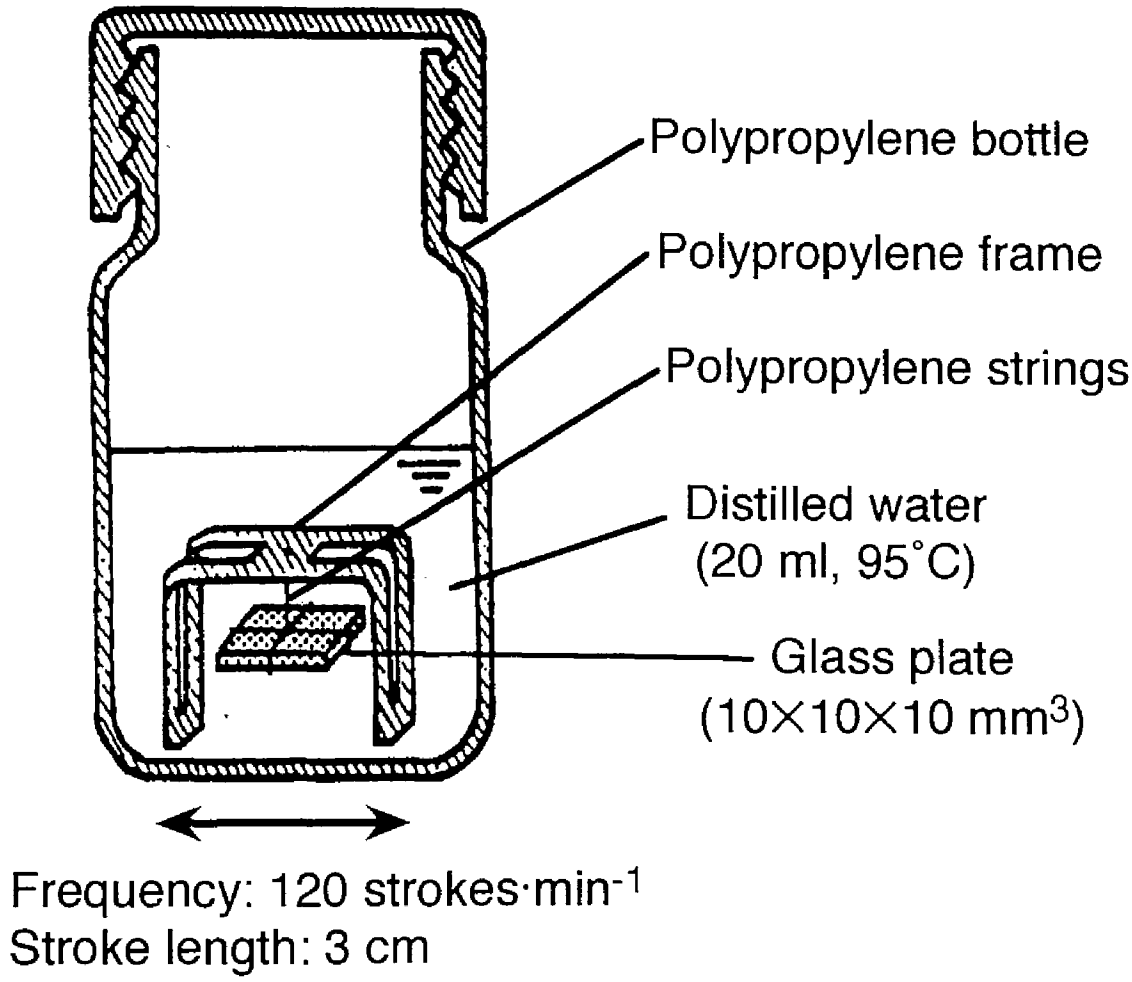

Figure 3. Test of chemical durability of silica glass plates implanted with P^+ ions.

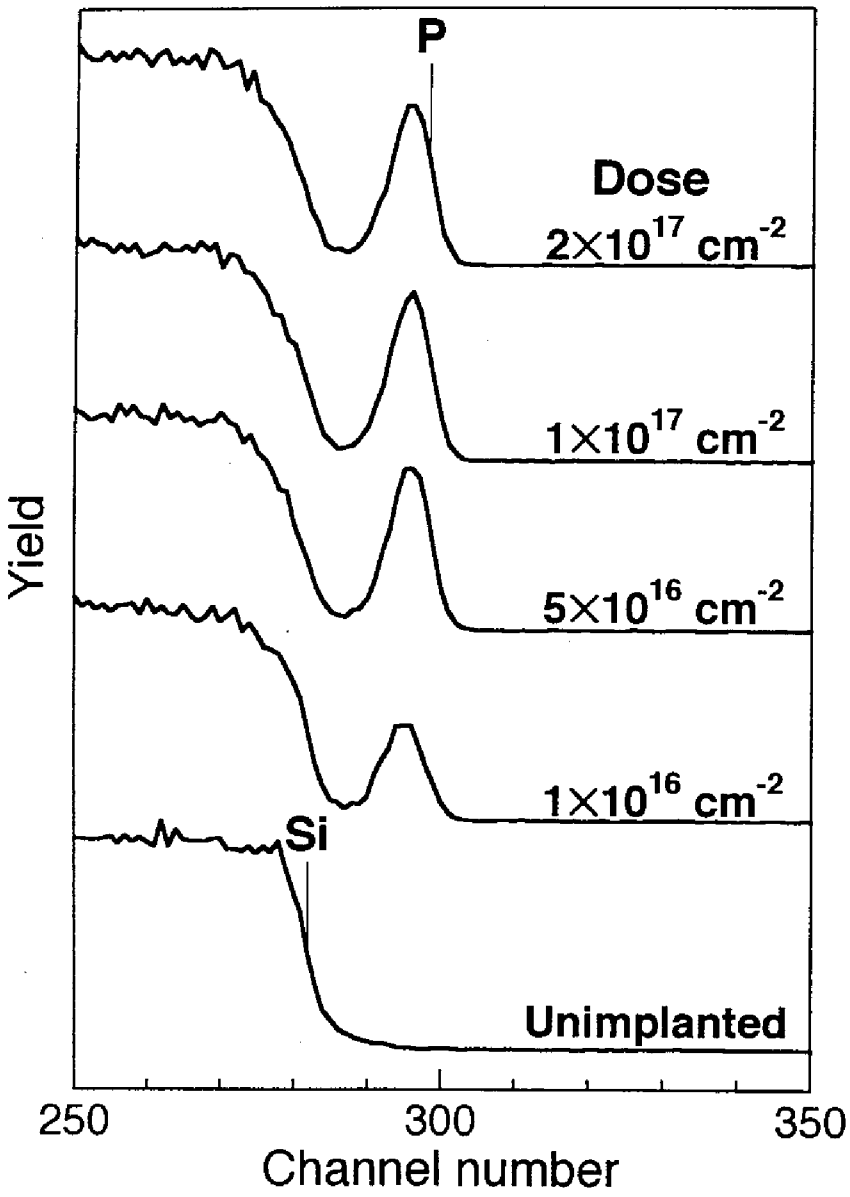

Figure 4. RBS spectra of silica glass plates implanted with P^+ ions at 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2}.

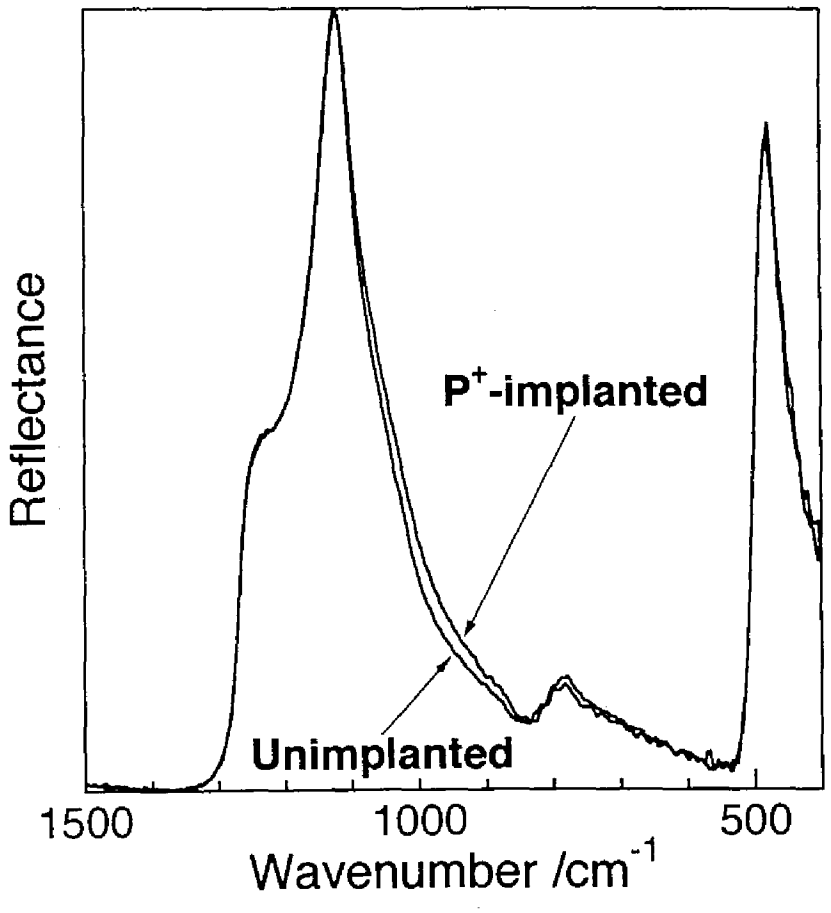

Figure 5. FT-IR reflection spectrum of a silica glass plate implanted with P^+ ions at 20 keV with a dose of 5×10^{16} cm^{-2}.

implanted with P^+ ions showed slightly larger reflectance compared with the unimplanted original glass in a region around 1,000 cm^{-1}.

Figure 6 shows the P_{2p} XPS spectra of silica glass implanted with P^+ ions at 20 keV with a dose of 5×10^{16} cm^{-2}. Two peaks at 130 and 134 eV were observed at the top surface. The binding energies of 130 and 134 eV coincide with those for elemental red phosphorus and oxidized phosphorus in hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), respectively. With increasing depth, the peak intensity ascribed to the elemental phosphorus increased while that ascribed to the oxidized phosphorus decreased. Only the peak of elemental phosphorus appeared for deeper regions than about 1.2 nm.

Figure 7 shows the concentrations of phosphorus and silicon dissolved from silica glass implanted with P^+ ions at 20 keV with various doses and soaked in water at 95°C for 7 days. The original silica glass released only a small amount of silicon and no phosphorus, whereas all the silica glasses implanted with P^+ ions with doses of 1×10^{16} to 2×10^{17} cm^{-2} released appreciable amounts of the phosphorus as well as the silicon.

Figure 8 shows the RBS spectrum of silica glass implanted with P^+ ions at 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2} and soaked in distilled water at 95°C for 7 days. For all the investigated doses, no peak of phosphorus was observed after the soaking.

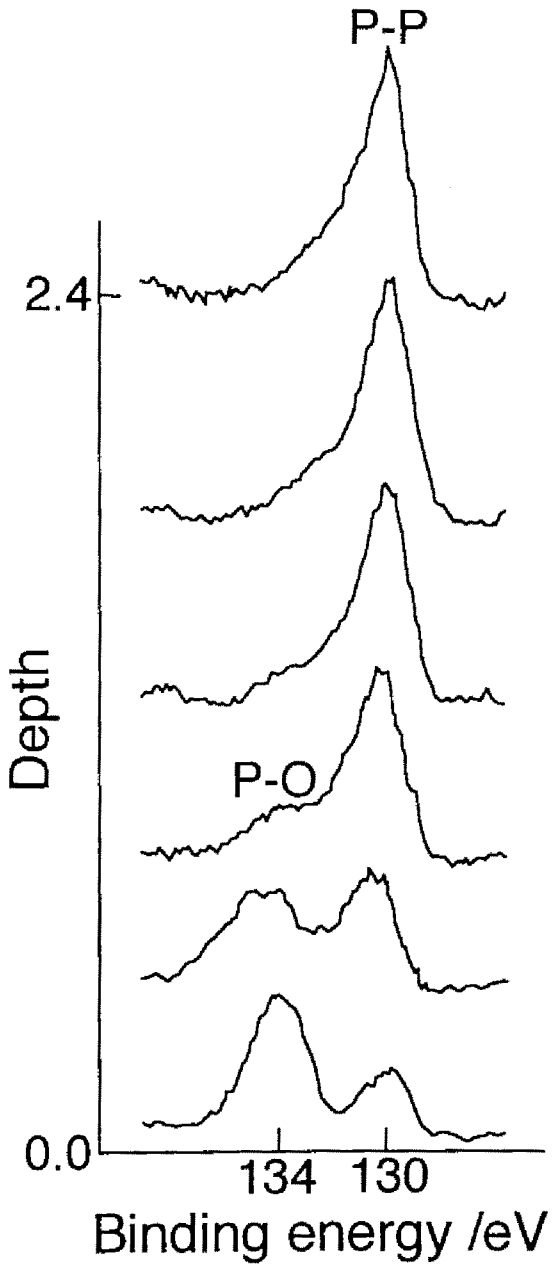

Figure 6. XPS spectra of a silica glass plate implanted with P^+ ions at 20 keV with a dose of 5×10^{16} cm^{-2}.

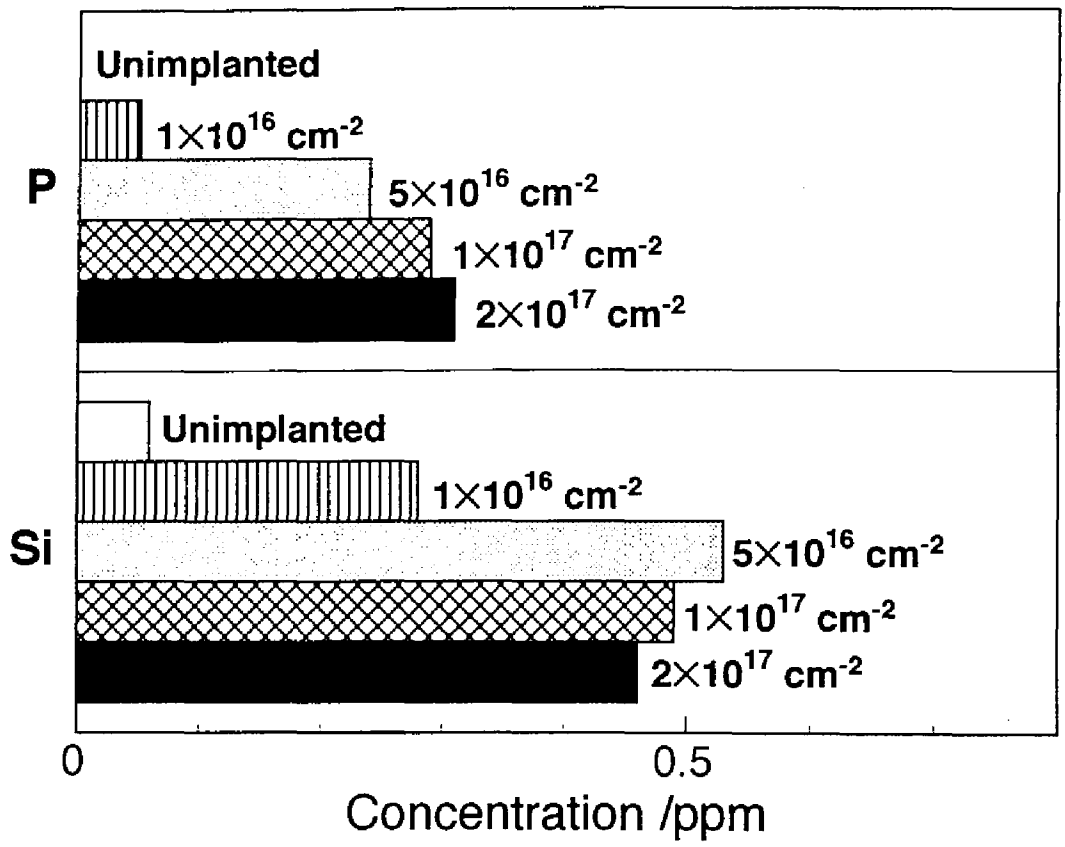

Figure 7. Concentrations of phosphorus and silicon released from silica glass plates implanted with P^+ ions at 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2} and soaked in water at 95°C for 7 days.

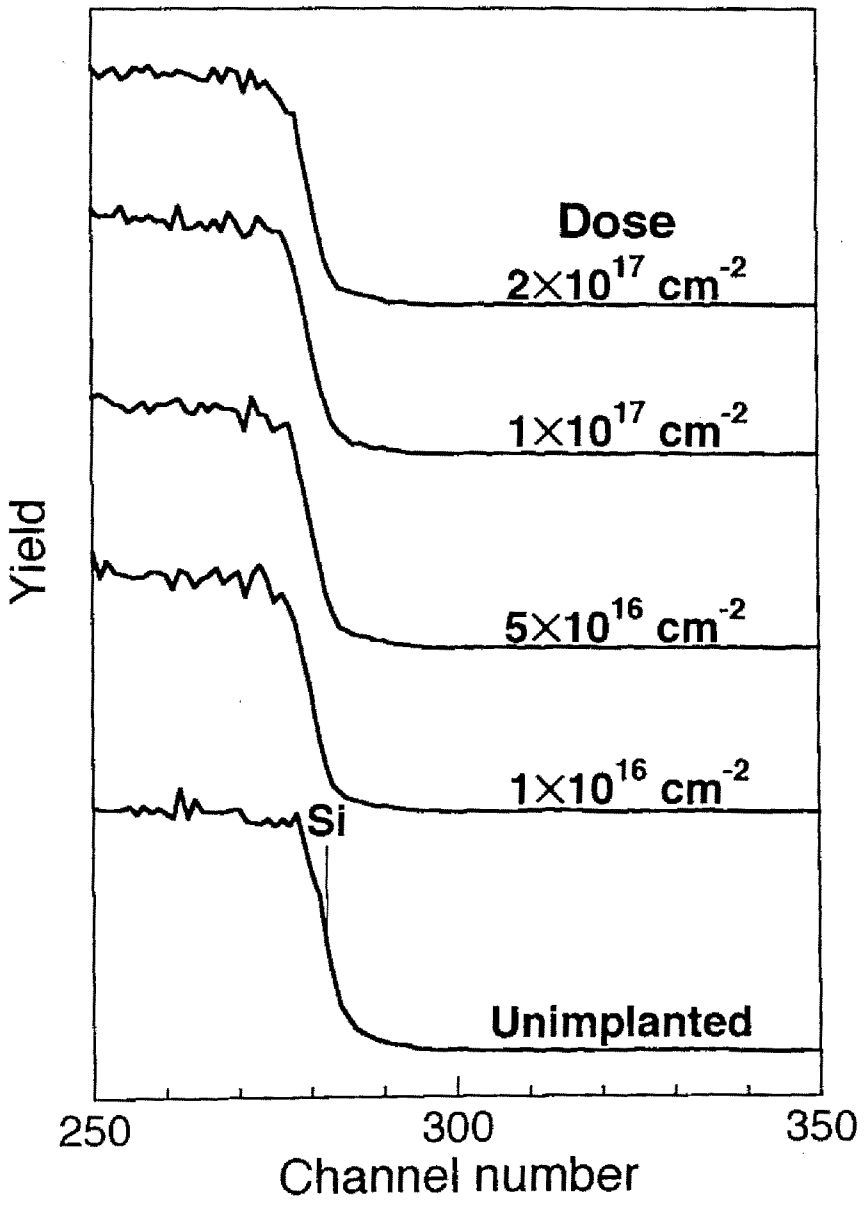

Figure 8. RBS spectra of silica glass plates implanted with P^+ ions at 20 keV with a dose of 5×10^{16} cm^{-2} dose and soaked in water at 95°C for 7 days.

4. Discussion

It can be seen from Fig. 4 that the amount of phosphorus implanted into the silica glass is saturated at a dose of 5×10^{16} cm^{-2} under the acceleration energy of 20 keV.

As shown in Fig. 5, the reflectance in a region around 1,000 cm^{-1} slightly increased by the ion implantation. This increase that structural damage was produced by the ion implantation, which is represented as the decrease in Si-O-Si bridging angle between SiO_4 tetrahedra [15-17].

Most of phosphorus implanted into the silica glass exists in a form of elemental phosphorus [18] for all the examined doses at 20 keV, although a part of the phosphorus is oxidized by the atmospheric oxygen at the surface of the glass for a dose of 5×10^{16} cm^{-2} (See Fig. 6). A silica glass was colored brown by the phosphorus ion implantation. This coloration may be attributed to the existence of the phosphorus colloid [18] in this glass.

The glasses implanted with all the investigated doses release appreciable amounts of phosphorus and silicon into hot water as shown in Fig. 7. It is assumed that all the implanted phosphorus was completely released from the glass into the hot water by the soaking, because no peak of phosphorus was observed for silica glasses implanted with P^+ ions and soaked into the hot water for 7 days (See Fig. 8). This appreciable releases of these elements are attributed to the presence of phosphorus in oxide form (See Fig. 6) at the surface of the glass, since phosphorus oxide

is known to hygroscopic [19].

It can be seen from these results that phosphorus ion implantation at energies higher than 20 keV, is required for obtaining silica glass with high phosphorus content as well as with high chemical durability, since an ion implantation at a higher energy could localize the phosphorus ions in deeper regions to prevent the distribution of phosphorus up to the surface and the subsequent oxidation of phosphorus. Thus prepared phosphorus-containing glass is believed to be useful for *in situ* radiotherapy of cancer, since phosphorus-31 in this glass can be activated to β-emitter ^{32}P with a half-life of 14.3 days.

5. Summary

P^+ ion implantation into silica glass plates was attempted at the acceleration energy of 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2}. The amount of phosphorus implanted into a silica glass was saturated at about a dose of 5×10^{16} cm^{-2} under 20 keV. Structural damage in the Si-O-Si network was produced at the glass surface by the ion implantation. The implanted phosphorus formed elemental phosphorus in a form of colloids in the glass and a part of it near the surface was oxidized by the atmospheric oxygen. The glasses implanted with P^+ ions at 20 keV released appreciable amounts of phosphorus and silicon into the hot water

within 7 days. Such low chemical durability of the glass was attributed to the presence of oxidized phosphorus at the surface of the glass.

For obtaining a silica glass with high chemical durability as well as with high phosphorus content, P^+ ion must be implanted at higher energies than 20 keV in order to prevent the distribution of the phosphorus to the glass surface and the subsequent formation of chemically less durable oxidized phosphorus at the glass surface.

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CHAPTER 2

STRUCTURE AND PROPERTIES OF SILICA GLASS PLATES IMPLANTED WITH P^+ IONS AT 50 keV

1. Introduction

Radiotherapy is one of the effective treatments of cancers without excising the host organ. Irradiation is, however, generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it is recently reported that a glass microsphere of 20 to 30 μm in diameter of $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition is useful for *in situ* irradiation of cancers [1-4]. Yttrium-89 (100% natural abundance) in this glass is activated β-emitter with a half-life of 64.1 h by neutron bombardment. Although ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) are also activated to β-emitters, the half-lives of the activated ^{28}Al and ^{31}Si are only 2.52 min. and 2.62 h, respectively [5]. Other silicons and oxygen are not activated by the neutron bombardment. Microspheres in the given sizes can directly irradiate cancer with short-ranged highly ionizing β-ray, when they are injected into the tumors

through blood vessels. The radioactivity of this glass, however, may result in the substantial decay even before the cancer treatment, because even ^{90}Y has a short half-life of 64.1 h [5].

Phosphorus-containing glass with high chemical durability is believed to be useful for *in situ* radiotherapy, since ^{31}P (100% natural abundance) in this glass can be activated to β-emitter ^{32}P with a half-life of 14.3 days by the neutron bombardment [5]. Phosphorus-rich glasses, however, generally show low chemical durabilities [6]. Glasses with high phosphorus content as well as with high chemical durability are expected to be prepared when phosphorus ion is implanted into a pure silica glass which is well known to show a high chemical durability.

In Chapter 1, the phosphorus ion implantation into highly pure silica glass plates was attempted under an acceleration energy of 20 keV. It was revealed that the amount of phosphorus is saturated at a dose of about 5×10^{16} cm^{-2} under 20 keV, and that the glass releases appreciable amounts of phosphorus and silicon into hot water even at a low dose of 1×10^{16} cm^{-2}. This significant release of the elements from the glass may be attributed to the formation of chemically less durable oxidized phosphorus at the glass surface.

In this chapter, P^+ ion implantation into a silica glass at 50 keV, which is little higher than 20 keV, with various doses was attempted in order to obtain the glass with not only high phosphorus content but also with high chemical durability. The chemical durability of the P^+-

implanted glasses in relation to their surface structural change due to the ion implantation were compared with those of 20 keV implantation in Chapter 1.

2. Experimental

2.1. P^+ Ion Implantation into Silica Glass Plates

Highly pure silica glass (metallic impurities < 0.5 ppm, OH < 100 ppm) prepared by vapor-phase axial deposition (SUMIQUARTZ SK-1300, Sumitomo Metal Industries Ltd., Tokyo, Japan) was cut into a rectangular specimens 10 mm×10 mm×1 mm in size, polished with diamond paste and annealed at 1100°C in a SiC electric furnace in order to eliminate the strains. As shown in Fig. 2 in Chapter 1, phosphorus ion (P^+) was generated by thermoelectron bombardment to red phosphorus vapor, and implanted into the glass plates at 50 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2} by an ion implanter (NH-20SR, Nissin Electrical Co. Ltd., Tokyo, Japan) at Ion Engineering Center Corporation, Osaka, Japan. The phosphorus ions was implanted intermittently into the samples which were scanned back and forth behind the window of 2 cm×8 cm in size. The mean beam current density in this window was 62.5 to 125 $\mu A \cdot cm^{-2}$. The temperatures of the samples rose by the ion implantation, but did not exceed 100°C. It is estimated theoretically that the phosphorus

implanted into the silica glass at implantation energy of 50 keV shows Gaussian distribution giving the maximum concentration at 48.6 nm in depth from the surface [7]. After the ion implantation, every sample was preserved in a dry nitrogen atmosphere to avoid the surface oxidation of the phosphorus.

2.2. Analysis of Glass Surface

The content of the phosphorus implanted into the glass was measured by a Rutherford Backscattering Spectrometry (RBS) with ion beam analyzer at Radiation Laboratory of Nuclear Engineering, Kyoto University, using 2 MeV $^4He^+$ ions with 170° incident angle. The state of phosphorus was investigated by measuring P_{2p} binding energy with an X-ray photoelectron spectroscope (XPS) (MT-5500, ULVAC-PHI Co. Ltd., Chigasaki, Japan), using MgKα (1253.6 eV) X-ray as an excitation source in the 10^{-9} Pa residual pressure range. The photoelectron take-off angle (the angle between the sample surface and the detector axis) was set at 45°. Xenon-ion sputtering was carried out at 4 keV to measure the depth profiles. The sputtered depth was determined by referring the sputtering rate, 0.12 nm·min^{-1}, of a SiO_2 film 0.35 nm thick formed on a silicon wafer. Measured binding energies were corrected by referring the binding energy of C_{1s} of the hydrocarbon (284.6 eV) adsorbed on the sample surfaces. Surface structures of the glasses were analyzed by a Fourier transform infrared attenuated total reflection (FT-IR ATR) spectrometer (System

2000 FT-IR, Perkin-Elmer Ltd., Buckinghamshire, England) with 45° incident angle, using KRS-5 as an internal reflection element.

2.3. Chemical Durability Test

The glasses implanted with P^+ ions were immersed into 20 ml of distilled water at 95°C in a polypropylene bottle, and shaken at a rate of 120 strokes·min^{-1} with a stroke length of 3 cm, as shown in Fig. 3 in Chapter 1. After 7 days, the concentrations of phosphorus and silicon released from the glasses into the hot water were measured by an inductively coupled plasma (ICP) atomic emission spectrometer (SPS-1500 VR, Seiko Instruments Inc., Tokyo, Japan).

3. Results

Figure 1 shows the RBS spectra of silica glass plates implanted with P^+ ions at 50 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2}. The area of the peak ascribed to the phosphorus increased with increasing dose up to 5×10^{17} cm^{-2} and slightly decreased for a dose of 1×10^{18} cm^{-2}. This indicates that the amount of the phosphorus implanted to a silica glass was nearly saturated at a dose of 5×10^{17} cm^{-2} and further implantation of the phosphorus sputtered out the previously implanted phosphorus.

Figure 2 shows the FT-IR ATR spectra of silica glass plates

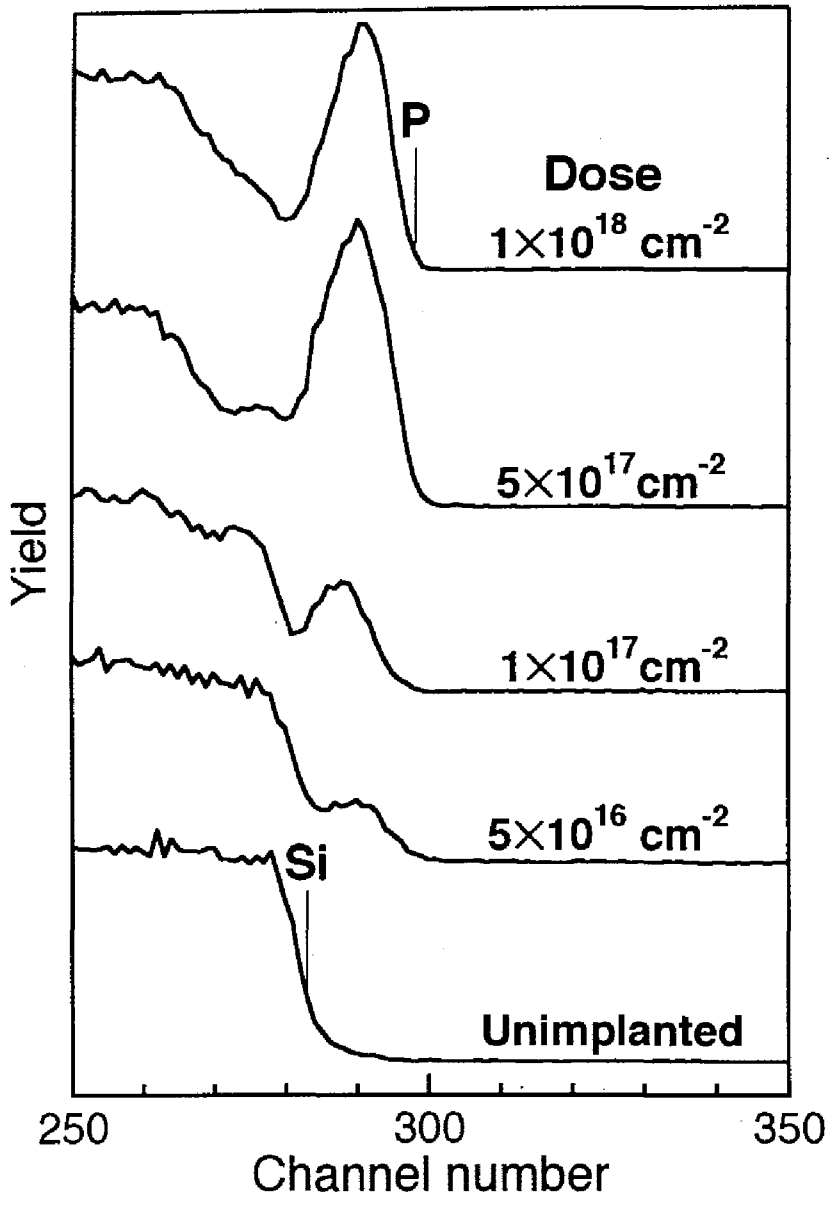

Figure 1. RBS spectra of silica glass plates implanted with P^+ ions at 50 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

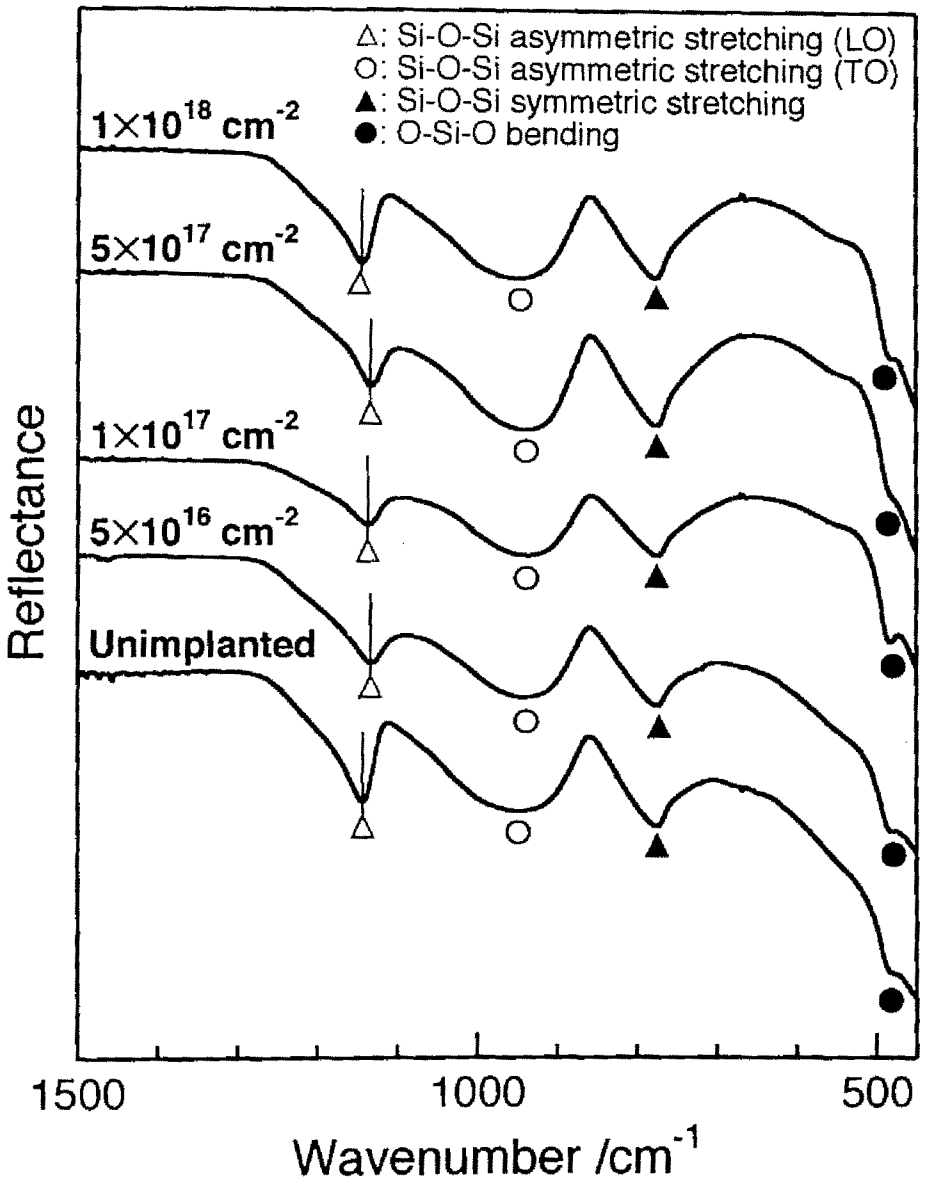

Figure 2. FT-IR ATR spectra of silica glass plates implanted with P^+ ions at 50 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

implanted with P^+ ions at 50 keV with various doses. Four peaks were observed at about 490 (●), 780 (▲), 900 (○) and 1150 (△) cm^{-1} for all the glasses. These bands are assigned to O-Si-O bending vibration, Si-O-Si symmetric stretching vibration, Si-O-Si asymmetric stretching vibration (transverse optical mode), Si-O-Si asymmetric stretching vibration (longitudinal optical mode), respectively [8-10]. The peak at 1150 cm^{-1} shifted to a lower wavenumber by the ion implantation.

Figure 3 shows the P_{2p} XPS spectra of silica glass plates implanted with P^+ ions at 50 keV with various doses. For a dose of 5×10^{16} cm^{-2} ((a)), no peak was observed at the surface, and only one peak at 130 eV was observed at the regions deeper than about 1.2 nm. This binding energy of 130 eV coincided with that for red phosphorus. The glass was colored brown. This means that the implanted phosphorus exists as colloids in this glass [11]. For doses larger than 1×10^{17} cm^{-2} ((b)-(d)), two peaks at 130 and 134 eV were observed at the surfaces. The binding energy of 134 eV coincided with that for oxidized phosphorus in hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). With increasing depth, the intensity of the peak ascribed to the elemental phosphorus increased while that ascribed to the oxidized phosphorus decreased. The amounts of the oxidized phosphorus at the surface as well as the colloidal phosphorus in the deeper region increased with increasing doses of the implanted phosphorus.

Figure 4 shows the concentrations of the phosphorus and silicon released from the glass plates implanted at 50 keV with various doses into

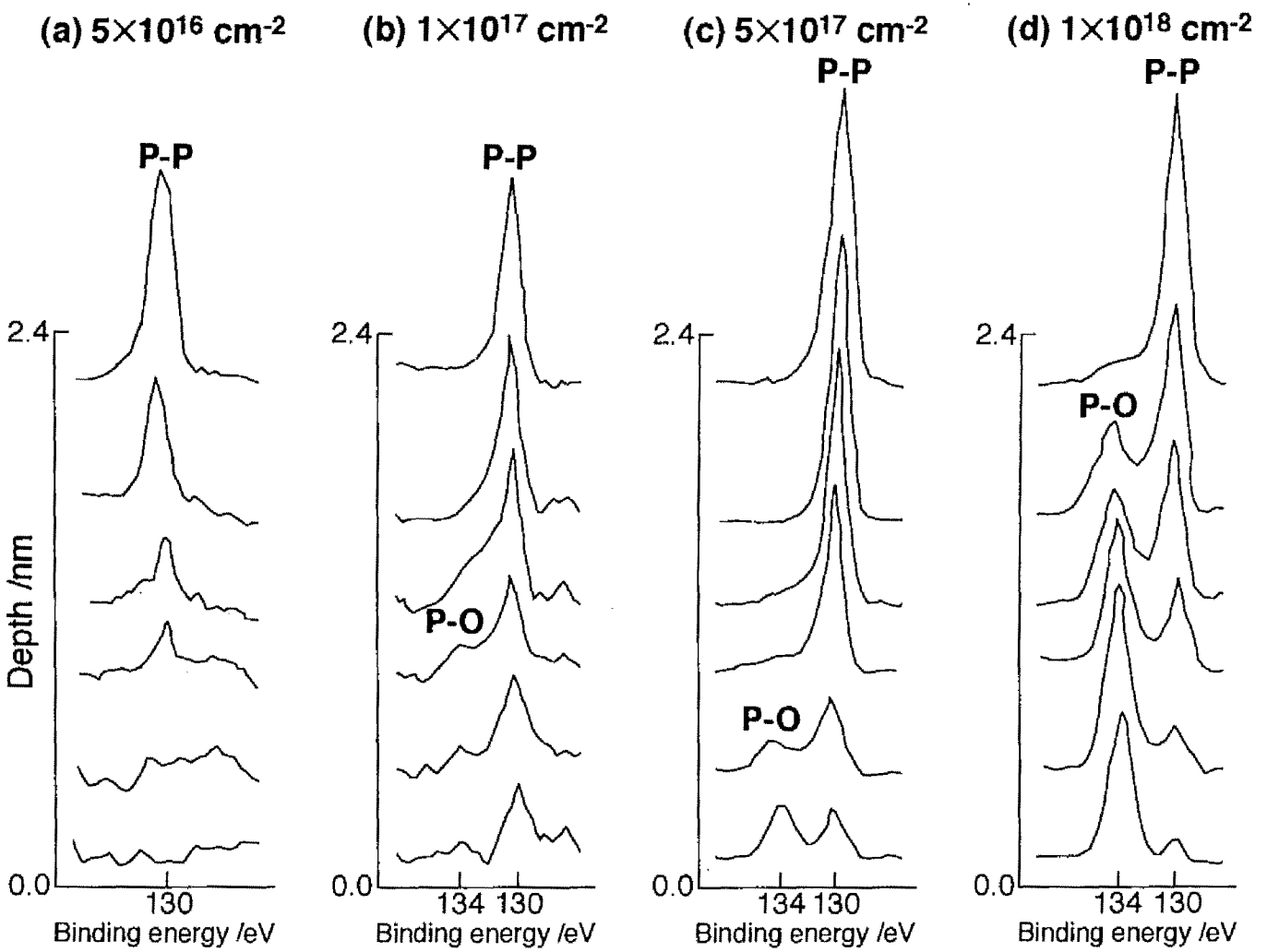

Figure 3. P_{2p} XPS spectra of silica glass plates implanted with P^+ ions at 50 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

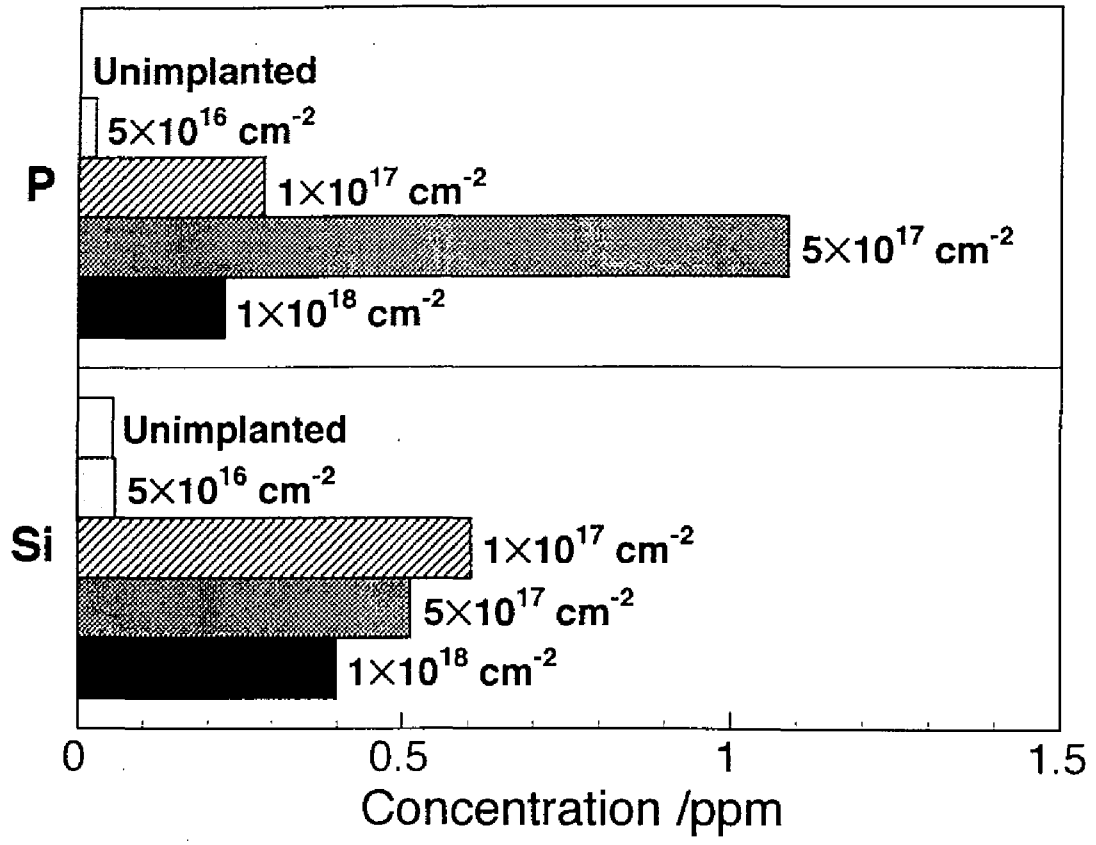

Figure 4. Concentrations of phosphorus and silicon released from silica glass plates implanted at 50 keV with various doses and soaked in water at 95°C for 7 days.

water at 95°C for 7 days. The glass implanted with a dose of 5×10^{16} cm^{-2} little released phosphorus and silicon, whereas those implanted with doses above 1×10^{17} cm^{-2} released appreciable amounts of both the elements.

Figure 5 shows the RBS spectra of silica glass plates implanted with P^+ ions at 50 keV with a dose of 5×10^{16} cm^{-2} before and after soaking in water at 95°C for 7 days. Calculated from the area of the peak ascribed to the phosphorus, it is confirmed that about 60% of the implanted phosphorus remained in the sample even after the soaking.

4. Discussion

As shown in Fig. 1, the amount of phosphorus was saturated for a dose of 5×10^{17} cm^{-2}. This saturation amount of the phosphorus in the glass is larger than that under an implantation energy of 20 keV where it was saturated at a dose of 5×10^{16} cm^{-2}. This can be explained by assuming that the implanted phosphorus can penetrate into deeper region at 50 keV (48.6 nm) than 20 keV (19.9 nm) [7].

The peak shifts of 1150 cm^{-1}-band to lower wavenumber in FT-IR ATR spectra (See Fig. 2) indicate that structural damages, represented as the decrease in Si-O-Si bond angle between SiO_4 tetrahedra [10, 12], are produced at the glass surface by the ion implantation, similar to 20 keV. The implanted phosphorus was localized in the region deeper than about

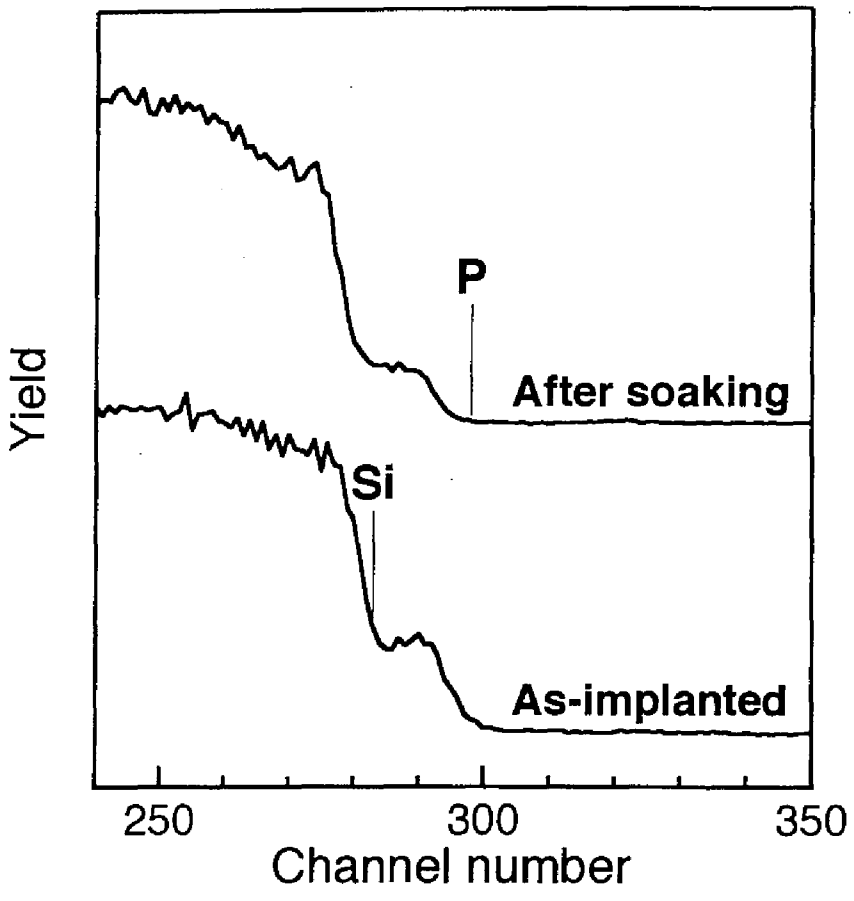

Figure 5. RBS spectra of silica glass plates implanted with P^+ ions at 50 keV with a dose of 5×10^{16} cm^{-2} before and after soaking in water at 95°C for 7 days.

1.2 nm for a dose of 5×10^{16} cm^{-2}, whereas it was distributed up to the surface and a part of it was oxidized at their surfaces for doses above 1×10^{17} cm^{-2}, as shown in Fig. 3. The results obtained is contrast with that under 20 keV where the phosphorus was distributed up to the surface to be oxidized at the surface even with a low dose of 5×10^{16} cm^{-2}. This is explained in terms of the increasing depth of the maximum concentration with increase in the acceleration energy.

The silica glass plate implanted with a dose of 5×10^{16} cm^{-2} little released both the phosphorus and silicon and retained the implanted phosphorus even after being soaked in water at 95°C for 7 days (See Fig. 5), whereas those implanted with doses above 1×10^{17} cm^{-2} released appreciable amounts of these elements into the hot water, as shown in Fig. 4. This indicates that the structural damage in the Si-O-Si network produced by the ion implantation gives no adverse effect on the chemical durability of the silica glass, and that no presence of phosphorus at the glass surface (See Fig. 3 (a)) is responsible for little release of both the elements from the glass implanted with a dose of 5×10^{16} cm^{-2}. The significant releases of the elements from the glasses implanted with doses above 1×10^{17} cm^{-2} are attributed to the presence of oxide of phosphorus (See Fig. 3 (b)-(d)), liable to be attacked by water [13], near the glass surfaces. At the acceleration energy of 20 keV, the silica glass implanted even with a low dose of 5×10^{16} cm^{-2} released significant amounts of phosphorus and silicon under the same condition, as shown in Chapter 1. This is contrast with the present results

at 50 keV described above.

In conclusion, the structural damage in the Si-O-Si network induced by the ion implantation gives no adverse effect on the high chemical durability of the silica glass, and the implanted phosphorus gives no detrimental effect on the chemical durability of the silica glass, when it is localized in a deep region from the surface, but does give it, when it is distributed to the surface to be oxidized. This indicates that a higher acceleration energy make the phosphorus to be localized in a deeper region of the glass to give a chemically durable glass containing a large amount of the phosphorus.

5. Summary

In this chapter, P^+ ion implantation into highly pure silica glass plates was performed at the acceleration energy of 50 keV, which is higher than 20 keV, with doses of 5×10^{16} to 1×10^{18} cm^{-2}. Under this acceleration energy, the amount of phosphorus in the glass was saturated at a dose of about 5×10^{17} cm^{-2}, which is higher dose than that under 20 keV. Structural damage in the Si-O-Si network was formed at the glass surface under 50 keV, similar to 20 keV. The implanted phosphorus was localized only in the regions deeper than 1.2 nm from the surface, taking a form of phosphorus colloids, for a dose of 5×10^{16} cm^{-2}, whereas it was distributed

up to the glass surface and a part of it near the surface was oxidized for doses above 1×10^{17} cm^{-2}. The former glass little released both the silicon and phosphorus into water at 95°C even after 7 days, whereas the latter glasses released appreciable amounts of these elements. This indicates that the structural damage in the Si-O-Si network induced by the ion implantation gives no adverse effect on the high chemical durability of the silica glass, and that the implanted phosphorus gives no detrimental effect on the chemical durability of the silica glass, when it is localized in a deep region from the surface, but does give it, when it is distributed to the surface to be oxidized. A higher acceleration energy make the phosphorus to be localized in a deeper region of the glass to give a chemically durable glass containing a large amount of the phosphorus.

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CHAPTER 3

STRUCTURE AND PROPERTIES OF SILICA GLASS PLATES IMPLANTED WITH P^+ IONS AT 100 keV

1. Introduction

Radiotherapy is one of the effective for cancer treatments without excising the host organ. Irradiation is, however, generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it is recently proposed that a glass microsphere of 20 to 30 μm in diameter of $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition is useful for *in situ* irradiation of cancers [1-4]. Yttrium-89 (100% natural abundance), ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) in this glass can be activated to β-emitters of ^{90}Y, ^{28}Al and ^{31}Si with half-lives of 64.1 h, 2.25 min. and 2.62 h by neutron bombardment, respectively [5]. Other silicons and oxygen are not activated by the neutron bombardment. When microspheres in the given sizes are injected into the tumors through blood vessels, they can directly irradiate cancer with short-ranged highly ionizing β-ray. The radioactivity of this glass,

however, may result in the substantial decay even before the cancer treatment, because even ^{90}Y has a short half-life of 64.1 h [5].

It is believed that phosphorus-containing glass with high chemical durability is useful for *in situ* radiotherapy, since ^{31}P (100% natural abundance) in this glass can be activated to β-emitter ^{32}P with a little longer half-life of 14.3 days by the neutron bombardment [5]. Glasses containing large amount of the phosphorus, however, generally show low chemical durabilities [6]. Glasses with high phosphorus content as well as with high chemical durability are expected to be obtained when phosphorus ion is implanted into a pure silica glass which is well known to show a high chemical durability.

In Chapters 1 and 2, phosphorus ion implantation into silica glass plates was attempted under acceleration energies of 20 and 50 keV, respectively. The silica glass plates implanted at 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2}, and those implanted at 50 keV with doses above 1×10^{17} cm^{-2}, however, released appreciable amounts of phosphorus and silicon into water at 95°C for 7 days. Such low chemical durabilities of these glasses were attributed to the formation of oxidized phosphorus near the glass surface.

In this chapter, acceleration energy of phosphorus ion implantation into silica glass plates was increased up to 100 keV in order to localize phosphorus in deeper region and obtain the glass with not only high phosphorus content but also with high chemical durability. The chemical

durability of the P^+-implanted glasses in relation to their surface structural change due to the ion implantation were compared with those of 20 and 50 keV implantation in Chapters 1 and 2.

2. Experimental

2.1. P^+ Ion Implantation into Silica Glass Plates

Highly pure silica glass (metallic impurities < 0.5 ppm, OH < 100 ppm) prepared by vapor-phase axial deposition (SUMIQUARTZ SK-1300, Sumitomo Metal Industries Ltd., Tokyo, Japan) was cut into a rectangular specimens 10 mm×10 mm×1 mm in size, polished with diamond paste and annealed at 1100°C in a SiC electric furnace in order to eliminate the strains. Phosphorus (P^+) ions were generated by thermoelectron bombardment to a red phosphorus vapor as shown in Fig. 2 in Chapter 1. The glass was implanted with P^+ ions at 100 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2} with an ion implanter (NH-20SR, Nissin Electrical Co. Ltd., Tokyo, Japan) at Ion Engineering Center Corporation, Osaka, Japan. It is estimated theoretically that the implanted phosphorus ion show Gaussian distribution giving the maximum concentration at 100.2 nm depth from the surface of the silica glass [7]. After ion implantation, every sample was preserved in a dry nitrogen atmosphere in order to prevent the surface oxidation of phosphorus.

2.2. Analysis of Glass Surface

The distribution of the phosphorus implanted into the glasses were examined by a Rutherford backscattering spectrometry (RBS) with ion beam analyzer at Radiation Laboratory of Nuclear Engineering, Kyoto University, using 2 MeV $^4He^+$ ions with 170° incident angle. The state of phosphorus was investigated by measuring P_{2p} binding energy with an X-ray photoelectron spectroscope (XPS) (MT-5500, ULVAC-PHI Co. Ltd., Chigasaki, Japan) using MgKα (1253.6 eV) X-ray as an excitation source in the 10^{-9} Pa residual pressure range. Xenon-ion sputtering was carried out at 4 keV to measure the depth profiles. Measured binding energies were corrected by referring the binding energy of C_{1s} of the hydrocarbon (284.6 eV) adsorbed on the sample surfaces. Surface structures of the glasses were analyzed by a Fourier transform infrared reflection (FT-IR) spectrometer (SR-5M, Japan Spectroscopic Co. Ltd., Tokyo, Japan) with 30° incident angle and a Fourier transform infrared attenuated total reflection (FT-IR ATR) spectrometer (System 2000 FT-IR, Perkin-Elmer Ltd., Buckinghamshire, England) with 45° incident angle.

2.3. Chemical Durability Test

The samples thus treated were soaked in 20 ml of distilled water at 95°C for 7 days in a polypropylene bottle, shaken at a rate of 120 strokes·min^{-1} with a stroke length of 3 cm, as shown in Fig. 3 in Chapter 1. The concentrations of phosphorus and silicon released from the glasses

were measured by an inductively coupled plasma (ICP) atomic emission spectrometer (SPS-1500 VR, Seiko Instruments Inc., Tokyo, Japan).

3. Results

Figure 1 shows the RBS spectra of silica glass plates implanted with P^+ ions at 100 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2}. The area of the peak ascribed to the phosphorus increased with increasing dose up to 5×10^{17} cm^{-2} and became almost constant for doses above 5×10^{17} cm^{-2}. This indicates that the amount of the phosphorus in the glass was saturated at a dose of about 5×10^{17} cm^{-2} at 100 keV, which is higher dose than that under 20 keV in Chapter 1 and similar dose to 50 keV in Chapter 2.

Figure 2 shows the FT-IR ATR spectra of silica glass plates implanted with P^+ ions at 100 keV with various doses. Four peaks were observed at about 490 (●), 780 (▲), 900 (○) and 1150 (△) cm^{-1} for all the glasses. These bands are assigned to O-Si-O bending vibration, Si-O-Si symmetric stretching vibration, Si-O-Si asymmetric stretching vibration (transverse optical mode), Si-O-Si asymmetric stretching vibration (longitudinal optical mode), respectively [8-10]. The peak at 1150 cm^{-1} was shifted to a lower wavenumber by the ion implantation.

Figure 3 shows the P_{2p} XPS spectra of silica glass plates implanted

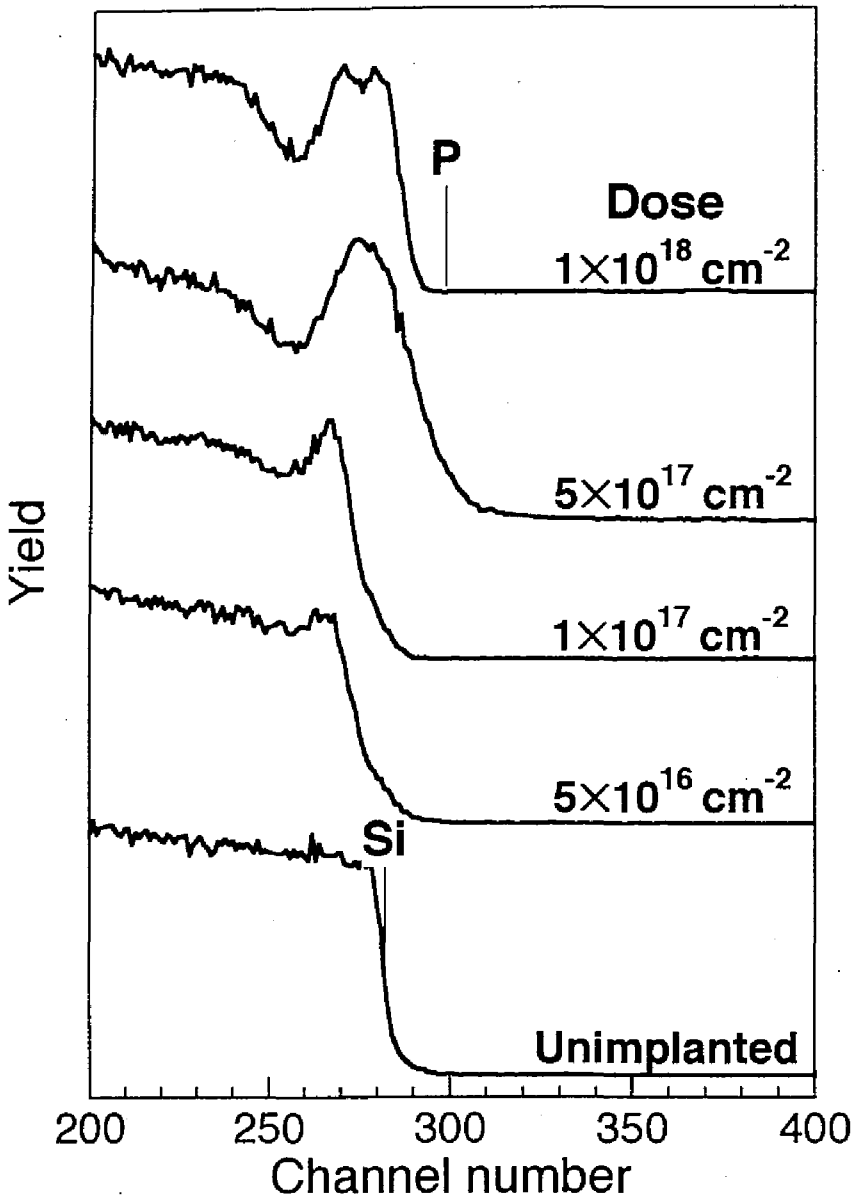

Figure 1. RBS spectra of silica glass plates implanted with P^+ ions at 100 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

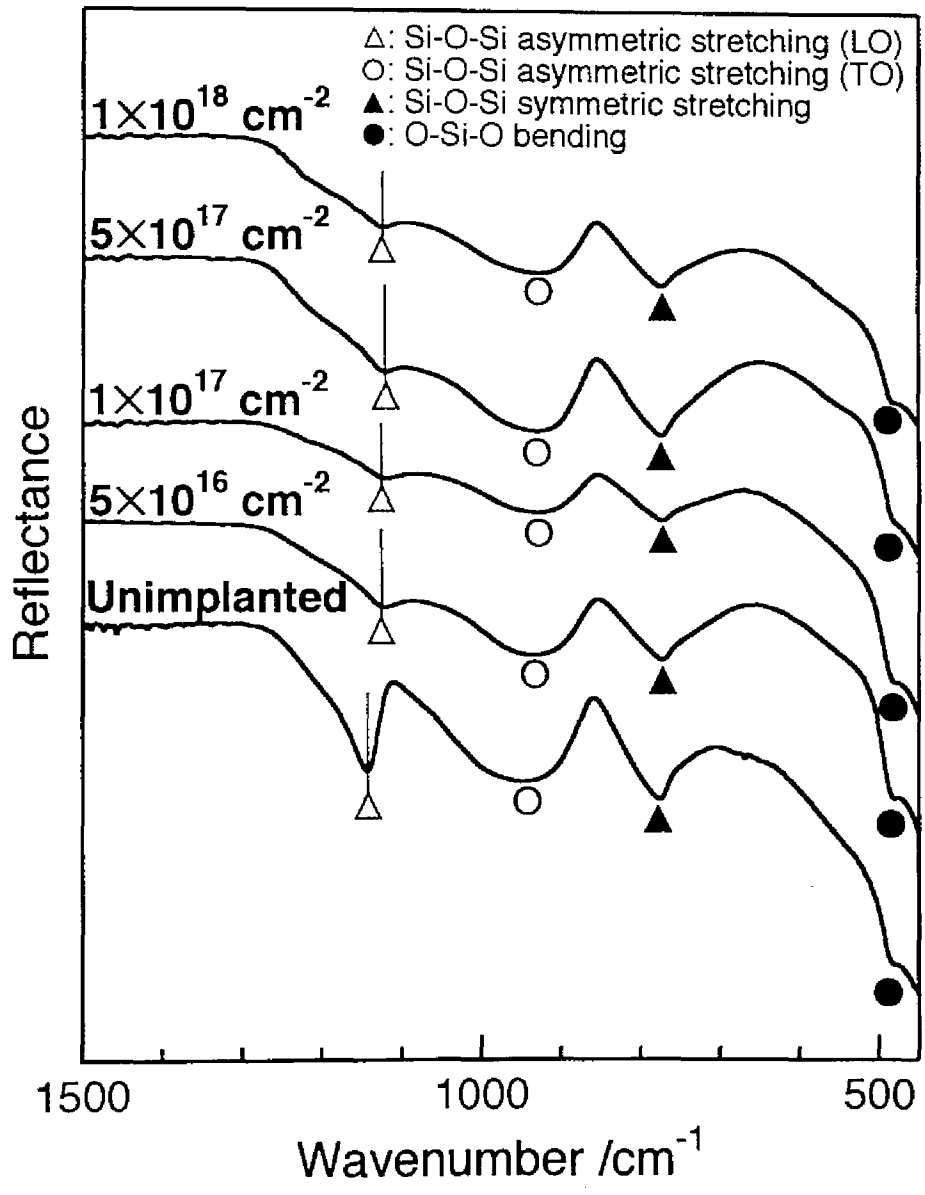

Figure 2. FT-IR ATR spectra of silica glass plates implanted with P^+ ions at 100 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

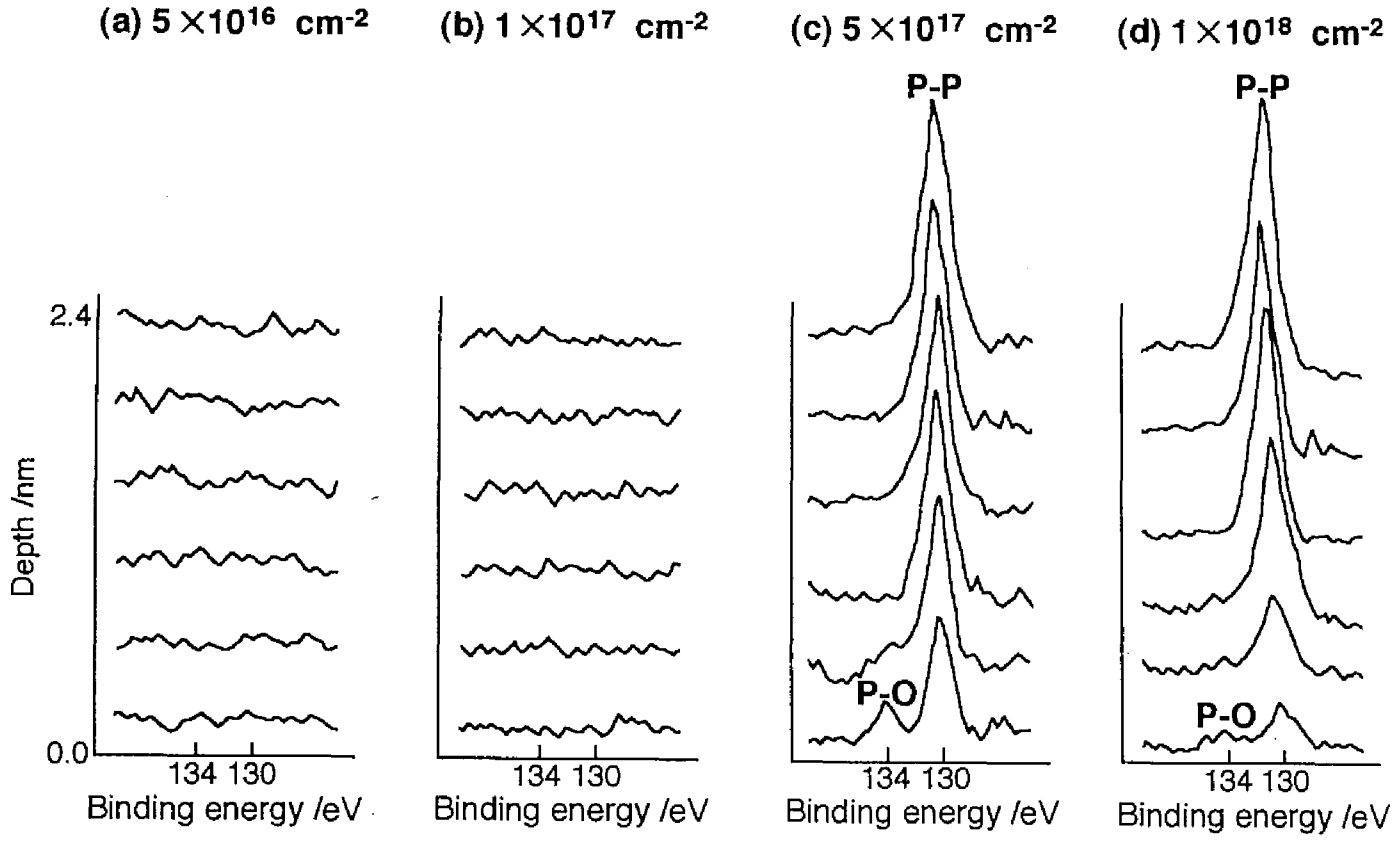

Figure 3. P_{2p} XPS spectra of silica glasse plates implanted with P^+ ions at 100 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

with P^+ ions at 100 keV with various doses. For doses of 5×10^{16} and 1×10^{17} cm^{-2} ((a) and (b)), no peak was observed from the glass surface down to a depth of 2.4 nm. For doses of 5×10^{17} and 1×10^{18} cm^{-2} ((c) and (d)), two peaks at 130 and 134 eV were observed from the glass surface. The binding energy of 130 eV coincided with that for elemental phosphorus, in red phosphorus, and the binding energy of 134 eV coincided with that for oxidized phosphorus, in hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), respectively. With increasing depth, the intensity of the peak ascribed to the elemental phosphorus increased while that ascribed to the oxidized phosphorus decreased.

Figure 4 shows the concentrations of the phosphorus and silicon released from the glass plates which was implanted with P^+ ions at 100 keV with various doses and soaked in water at 95°C for 7 days. The glasses implanted with doses of 5×10^{16} and 1×10^{17} cm^{-2} little released both of the phosphorus and silicon, whereas those implanted with doses 5×10^{17} and 1×10^{18} cm^{-2} released appreciable amounts of both the elements.

Figure 5 shows the RBS spectra of silica glass implanted with P^+ ions at 100 keV with a dose of 1×10^{17} cm^{-2} before and after soaking in water at 95°C for 7 days. It is confirmed from the area of the peak ascribed to the phosphorus that about 90% of the implanted phosphorus was retained in the glass even after the soaking. This result agrees with little release of phosphorus shown in Fig. 4.

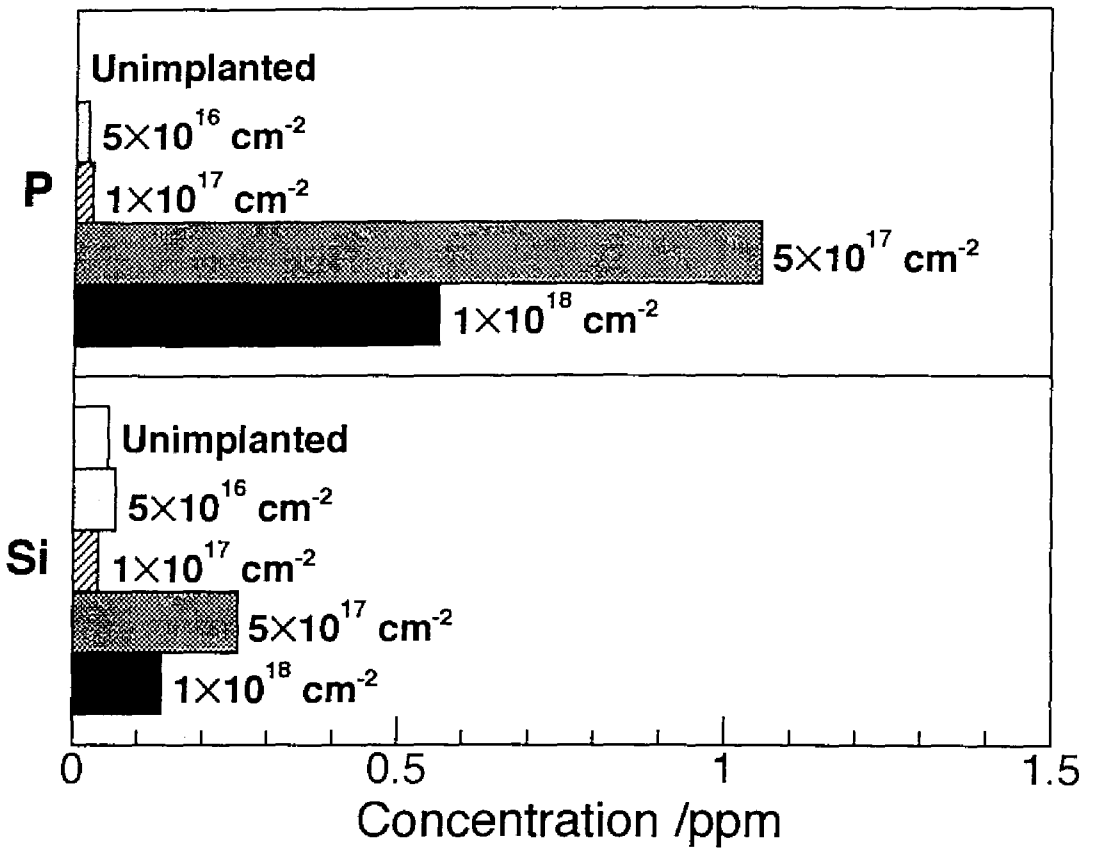

Figure 4. Concentrations of phosphorus and silicon released from silica glass plates implanted with P^+ ions at 100 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2} into water at 95°C for 7 days.

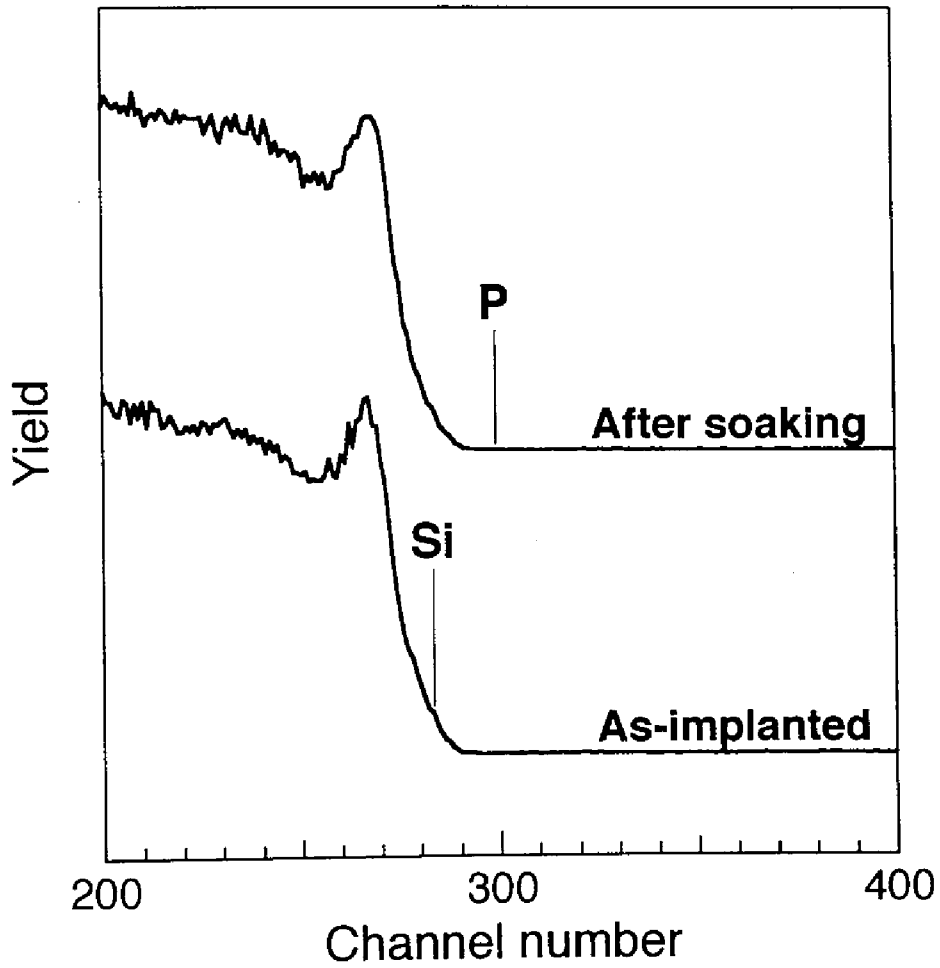

Figure 5. RBS spectra of silica glass plates implanted with P^+ ions at 100 keV with a dose of 1×10^{17} cm^{-2} before and after soaking in water at 95°C for 7 days.

4. Discussion

The amount of the phosphorus ions implanted into the silica glass saturated at a dose of 5×10^{17} cm^{-2} with 100 keV, which is larger than the 5×10^{16} cm^{-2} for the implantation energy of 20 keV in Chapter 1. This is explained by assuming that the implantation at 100 keV gives the maximum concentration of the phosphorus at a larger depth from the surface of the silica glass than for 20 keV in Chapter 1; i.e. the maximum concentrations of the phosphorus implanted at 20 and 100 keV are theoretically estimated to be located at depths of 19.9 and 100.2 nm, respectively [7].

As shown in Fig. 2, the peak at 1150 cm^{-1} of the silica glass was shifted to a lower wavenumber by the phosphorus ion implantation. This shift is attributed to the formation of structural damage, represented as a decrease in Si-O-Si bond angle at the surface of the glass [10, 11], similar to 20 and 50 keV implantation in Chapters 1 and 2.

Most of the phosphorus implanted into the silica glass exists in a form of the elemental phosphorus [12] for all the examined doses at 100 keV, although some of the phosphorus exists in a form of phosphorus oxide at the surface of the glass for doses above 1×10^{17} cm^{-2}. The silica glass was colored brown by the P^+ ion implantation. This means that this elemental phosphorus takes a form of the phosphorus colloid [12]. The phosphorus oxide at the surface of the glass for doses above 1×10^{17} cm^{-2} is

considered to be formed near the surface because the phosphorus ions were distributed up to the surface and oxidized by the atmospheric oxygen. For doses of 5×10^{16} and 1×10^{17} cm^{-2}, the phosphorus ions were not distributed up to the surface so as to reach the surface and hence the phosphorus oxide was not formed at the surface of the glass. At the acceleration energies of 20 and 50 keV described in Chapters 1 and 2, the phosphorus ions were distributed up to the surface of the glass and oxidized even for doses of 5×10^{16} and 1×10^{17} cm^{-2}, respectively. These results are explained in terms of the increasing depth of the maximum concentration with increase in the acceleration energy.

On the basis of these structural findings, the dependence of the release of the phosphorus and silicon from the silica glass into the hot water on the doses of ion implanted, shown in Fig. 4, is interpreted as follows. The silica glasses, implanted with P^+ ions at 100 keV with doses of 5×10^{16} and 1×10^{17} cm^{-2}, released little both of the phosphorus and silicon. The small amount of phosphorus released from these glasses is attributed to the no presence of the phosphorus at the surface of the glass (See Fig. 2 (a) and (b)). The release of silicon from these glasses was as little as that from the unimplanted silica glass (See Fig. 4). This indicates that the structural damage of the silica glass, formed by the ion implantation, has no adverse effect on the chemical durability of the silica glass. The silica glasses implanted with P^+ ions with doses above 5×10^{17} cm^{-2} released appreciable amount of the phosphorus as well as silicon. The appreciable releases of

these elements from these glasses are attributed to the presence of the phosphorus in oxide form at the surfaces of the glasses, since the phosphorus oxide is known to be hygroscopic [13].

As shown in Chapters 1 and 2, at 20 and 50 keV, even the silica glass implanted with doses as low as 5×10^{16} and 1×10^{17} cm^{-2} released appreciable amounts of the phosphorus and silicon. This is in contrast with the present results at 100 keV.

The number of the phosphorus ions present in a microsphere of 20 μm in diameter of silica glass implanted with P^+ ions with a dose of 1×10^{17} cm^{-2}, which has a high chemical durability, is 2.09×10^{-12} mol, whereas that of yttrium ions present in one microsphere in the same size of the glass of the composition $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%), which is already clinically used for the radiotherapy, is 4.88×10^{-11} mol. Therefore, P^+ ion must be implanted at a higher energy in order to obtain a chemically durable silica glass containing the phosphorus in the amount comparable to the yttrium in the Y_2O_3-Al_2O_3-SiO_2 glass.

In conclusion, the amount of phosphorus in the glass was saturated at a dose of about 5×10^{17} cm^{-2}, similar to under 50 keV. Little phosphorus was present in the surface region, at least to a depth of 2.4 nm even for a dose of 1×10^{17} cm^{-2}, whereas an appreciable amount of it was distributed up to the glass surface and a part of it was oxidized for doses above 5×10^{17} cm^{-2}. The glasses implanted with doses below 1×10^{17} cm^{-2} hardly released both of the phosphorus and silicon into water at 95°C even after 7 days,

whereas the glasses implanted with doses above 5×10^{17} cm^{-2} released appreciable amounts of these elements. The number of the phosphorus ions present in the silica glass implanted with P^+ ions at a dose of 1×10^{17} cm^{-2} corresponds to only about 10% the number of the yttrium ions in the $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass for one microsphere 20 μm in diameter. Therefore, P^+ ion must be implanted at a higher energy in order to obtain a chemically durable silica glass containing the phosphorus in the amount comparable to the yttrium in the Y_2O_3-Al_2O_3-SiO_2 glass.

5. Summary

In this chapter, acceleration energy of P^+ ion implantation into silica glass plates was increased up to 100 keV. The amount of phosphorus in the glass was saturated at a dose of about 5×10^{17} cm^{-2}, similar to under 50 keV. Little phosphorus was present in the surface region, at least to a depth of 2.4 nm even for a dose of 1×10^{17} cm^{-2}, whereas an appreciable amount of it was distributed up to the glass surface and a part of it was oxidized for doses above 5×10^{17} cm^{-2}. The glasses implanted with doses below 1×10^{17} cm^{-2} hardly released both of the phosphorus and silicon into water at 95°C even after 7 days, whereas the glasses implanted with doses above 5×10^{17} cm^{-2} released appreciable amounts of these elements. The number of the phosphorus ions present in the silica glass implanted with P^+

ions at a dose of 1×10^{17} cm^{-2} corresponds to only about 10% of the number of the yttrium ions in the $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass for one microsphere 20 μm in diameter. Therefore, P^+ ion must be implanted at a higher energy in order to obtain a chemically durable silica glass containing the phosphorus in the amount comparable to the yttrium in the Y_2O_3-Al_2O_3-SiO_2 glass.

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CHAPTER 4

STRUCTURE AND PROPERTIES OF SILICA GLASS PLATES IMPLANTED WITH P^+ IONS AT 200 keV

1. Introduction

Radiotherapy is one of the effective for cancer treatments without excising the host organ. Irradiation is, however, generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it has been reported that a glass microsphere of 20 to 30 μm in diameter of $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition is useful for *in situ* irradiation of cancers [1-4]. Yttrium-89 (100% natural abundance), ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) in this glass can be activated to β-emitters of ^{90}Y, ^{28}Al and ^{31}Si with half-lives of 64.1 h, 2.25 min. and 2.62 h by neutron bombardment, respectively [5]. Other silicons and oxygen are not activated by the neutron bombardment. The radioactivity of this glass, however, may remarkably decreased even before the cancer treatment, because even ^{90}Y has a short half-life of 64.1 h [5].

A chemically durable glass containing a large amount of phosphorus is believed to be useful for *in situ* radiotherapy, since it can be activated to irradiate β-ray with a half-life of 14.3 days by the neutron bombardment [5]. It can be expected that phosphorus-containing glass with high chemical durability can be prepared by phosphorus ion implantation into a pure silica glass with high chemical durability.

In Chapter 3, it was shown that a phosphorus-containing silica glass with high chemical durability was obtained by phosphorus ion implantation at 100 keV with a dose of 1×10^{17} cm^{-2}. The number of the phosphorus ions present in this glass, however, corresponds to only about 10% of the number of the yttrium ions in the $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass for one microsphere 20 μm in diameter.

In this chapter, acceleration energy of P^+ ion implantation was furthermore elevated up to 200 keV, which is the highest energy available with the popular ion implanter commercialized, in order to prepare a chemically durable glass with high phosphorus content. The distribution and state of the implanted phosphorus, and surface structural change of the glass due to the ion implantation were examined together with an assessment of the chemical durability of the glasses implanted with P^+ ions in terms of their surface structures.

2. Experimental

2.1. P^+ Ion Implantation into Silica Glass Plates

Highly pure silica glass (metallic impurities < 0.5 ppm, OH < 100 ppm) prepared by vapor-phase axial deposition (SUMIQUARTZ SK-1300, Sumitomo Metal Industries Ltd., Tokyo, Japan) was cut into a rectangular specimens 10 mm×10 mm×1 mm in size, polished with diamond paste and annealed at 1100°C in a SiC electric furnace in order to eliminate the strains. As shown in Fig. 2 in Chapter 1, phosphorus (P^+) ion was generated by thermoelectron bombardment to a vapor of red phosphorus. The glass plate was implanted with P^+ ions at 200 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2} with an ion implanter (NH-40SR, Nissin Electrical Co. Ltd., Tokyo, Japan) at Ion Engineering Center Corporation, Osaka, Japan. It is estimated theoretically that the implanted phosphorus ion show Gaussian distribution giving the maximum concentration at 207.3 nm depth from the surface of the silica glass [8]. After ion implantation, every sample was preserved in a dry nitrogen atmosphere in order to prevent the surface oxidation of phosphorus.

2.2. Analysis of Glass Surface

The content of the phosphorus implanted into the glasses was measured by a Rutherford Backscattering Spectrometry (RBS). The ion beam analyzer at Radiation Laboratory of Nuclear Engineering, Kyoto

University, was used for the measurements with 2 MeV $^4He^+$ ions with a 170° incident angle.

The chemical state of phosphorus was investigated by measuring the P_{2p} binding energy with an X-ray photoelectron spectroscope (XPS) (MT-5500, ULVAC-PHI Co. Ltd., Chigasaki, Japan). MgKα (1253.6 eV) X-ray was used as an excitation source at the residual pressure of 10^{-9} Pa. The photoelectron take-off angle (the angle between the sample surface and the detector axis) was set at 45°. Xenon-ion sputtering was carried out at 4 keV to measure the depth profiles. The sputtered depth was determined by referring the sputtering rate, 0.12 nm·min^{-1}, of a SiO_2 film 0.35 nm thick formed on a silicon wafer. The measured binding energies were corrected with reference to the binding energy of C_{1s} (284.6 eV) of the hydrocarbon adsorbed on the sample surfaces.

The depth profile of the implanted phosphorus was measured by a Secondary Ion Mass Spectrometry (SIMS) (SIMS4000, Atomica Analysetechnik GMBH, München, Germany). The ^{31}P (100% natural abundance) and ^{18}O (20.4% natural abundance) signals were detected by Cs^+ primary beam with 0.5 μmϕ at 10 keV-100 nA. For each measurement point up to 1.5 μm depth, a 300 μm×300 μm square area was resolved into 256×256 mesh points. The intensity of ^{31}P signal was normalized by being divided that of ^{18}O signal in the silica glass matrix.

The cross section of the P^+-implanted silica glass was observed by a Transmission Electron Microscope (TEM) (H-700, Hitachi Ltd., Tokyo,

Japan) at 200 kV of the acceleration voltage of electron. The structure, i.e. crystalline or amorphous nature, of the implanted phosphorus was analyzed by a Micro Reflection High Energy Electron Diffraction (μRHEED) (H-700, Hitachi Ltd., Tokyo, Japan) with a beam diameter of 10 nmϕ.

The surface structure of the glass was analyzed with a Fourier transform infrared attenuated total reflection (FT-IR ATR) spectrometer (System 2000 FT-IR, Perkin-Elmer Ltd., Buckinghamshire, England) with a 45° incident angle, using KRS-5 as an internal reflection element.

2.3. Chemical Durability Test

The samples thus treated were soaked in 20 ml of distilled water at 95°C for 7 days in a polypropylene bottle, shaken at a rate of 120 strokes·min^{-1} with a stroke length of 3 cm, as shown in Fig .3 in Chapter 1. The concentrations of phosphorus and silicon released from the glasses were measured by an inductively coupled plasma (ICP) atomic emission spectrometer (SPS-1500 VR, Seiko Instruments Inc., Tokyo, Japan).

3. Results

Figure 1 shows the RBS spectra of silica glasses implanted with P^+ ions at 200 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2}. The area of the peak ascribed to the phosphorus increased with increasing

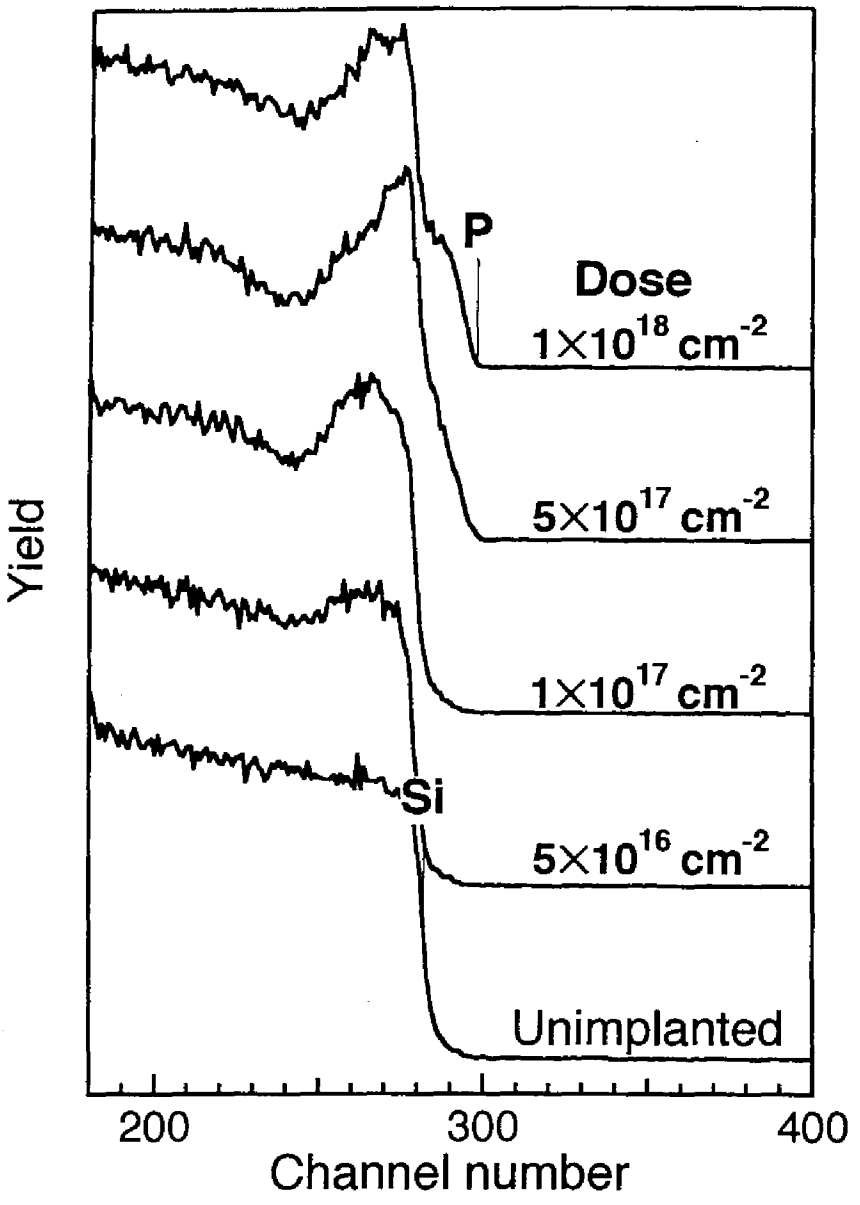

Figure 1 RBS spectra of silica glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

dose up to 1×10^{18} cm^{-2}, although the peak of phosphorus overlapped that of silicon.

Figure 2 shows the FT-IR ATR spectra of silica glasses implanted with P^+ ions at 200 keV with different doses. Four peaks were observed at about 490 (●), 780 (▲), 900 (○) and 1150 (△) cm^{-1} for all the glasses. These bands are assigned to O-Si-O bending vibration, Si-O-Si symmetric stretching vibration, Si-O-Si asymmetric stretching vibration (transverse optical mode), Si-O-Si asymmetric stretching vibration (longitudinal optical mode), respectively [8-10]. The peak at 1150 cm^{-1} was shifted to a lower wavenumber by the ion implantation.

Figure 3 shows the P_{2p} XPS spectra of silica glasses implanted with P^+ ions at 200 keV with various doses. For doses of 5×10^{16} and 1×10^{17} cm^{-2} ((a) and (b)), no peak was observed from the surface to a depth of 2.4 nm. For doses of 5×10^{17} and 1×10^{18} cm^{-2} ((c) and (d)), only one peak at 130 eV was observed near the glass surface. The binding energy of 130 eV coincided with that for elemental phosphorus in red phosphorus. The intensity of the peak ascribed to the elemental phosphorus is extremely small at the surface and increased with increasing depth.

Figure 4 shows the SIMS spectrum of the phosphorus in a silica glass implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}. The implanted phosphorus showed a considerably broad profile with its maximum concentration at 200-250 nm depth, which coincided with the calculated maximum concentration depth (207.3 nm) [7]. The phosphorus

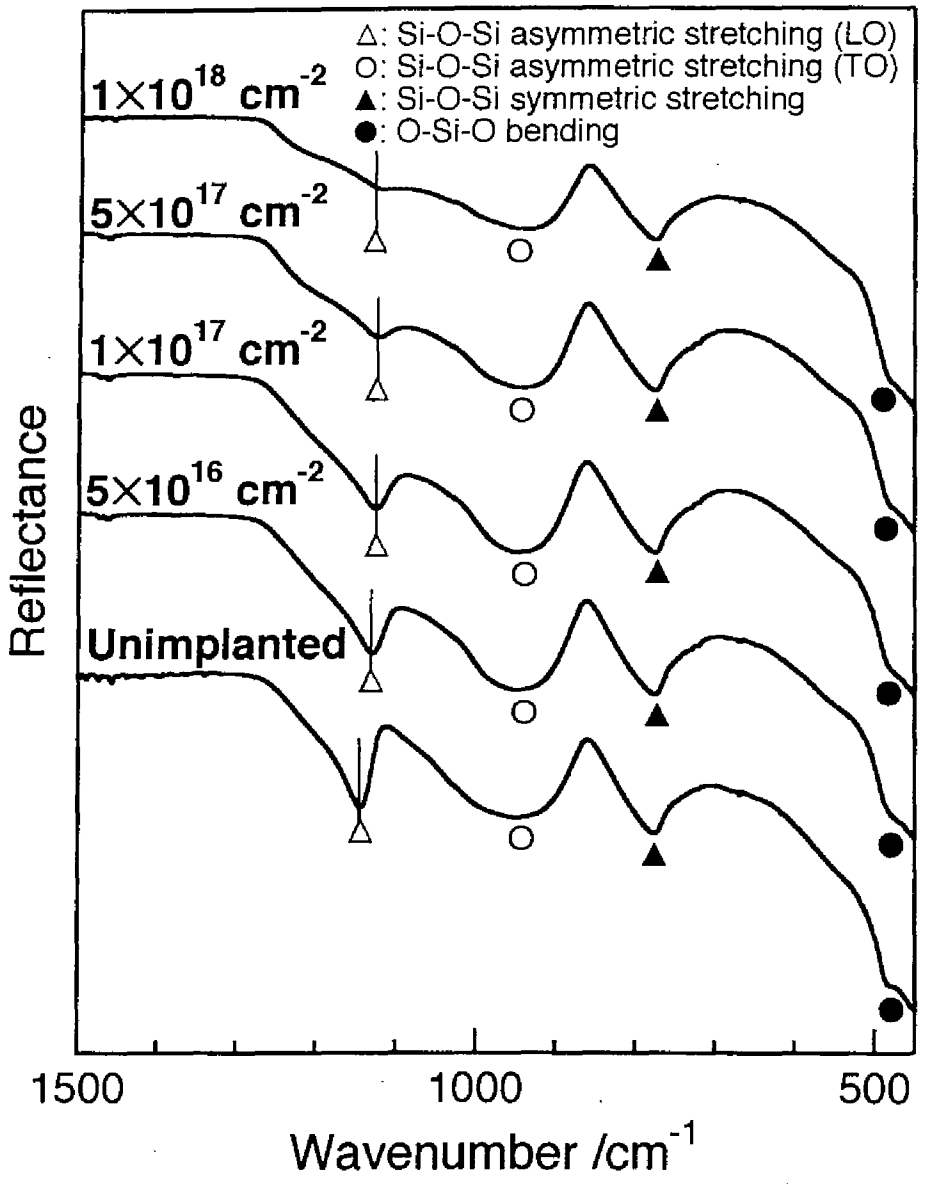

Figure 2. FT-IR ATR spectra of silica glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

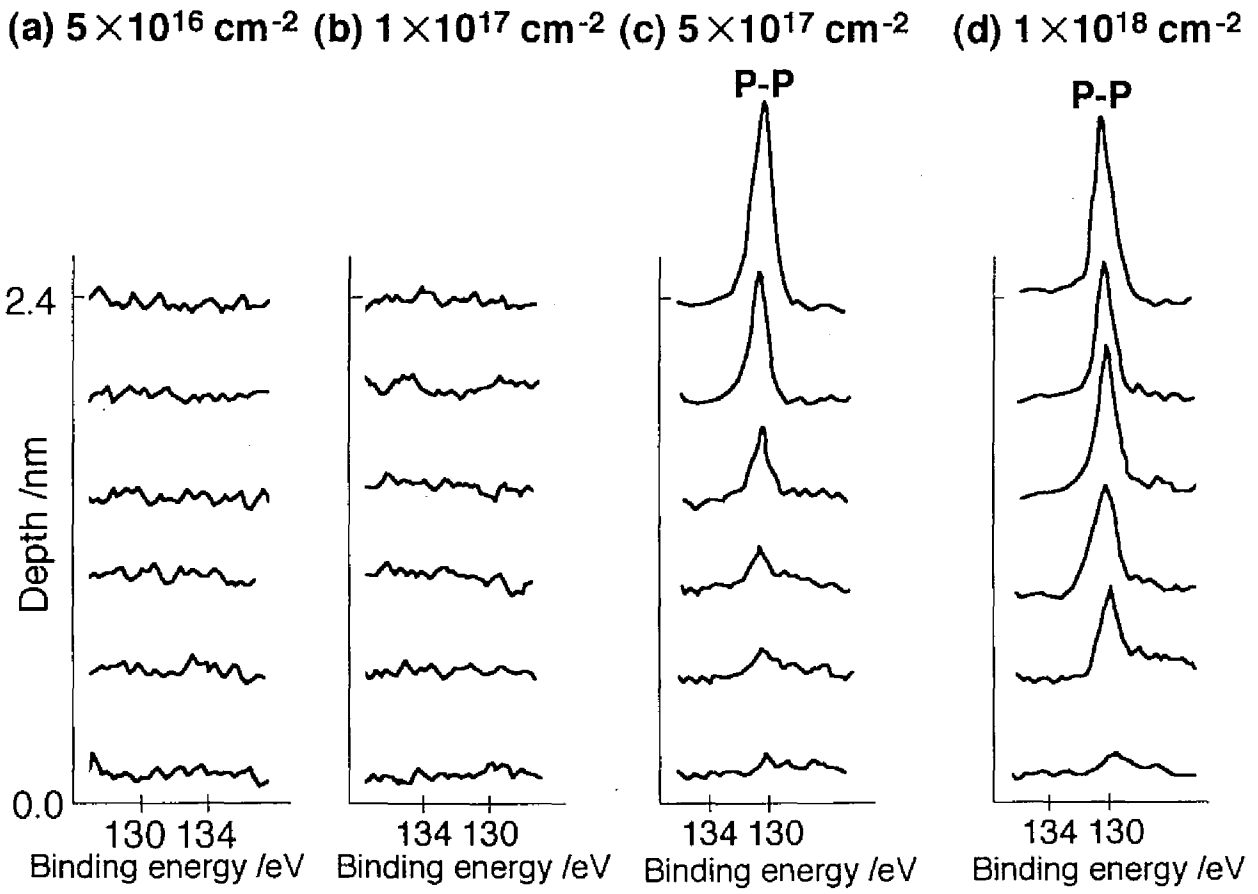

Figure 3. P_{2p} XPS spectra of silica plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

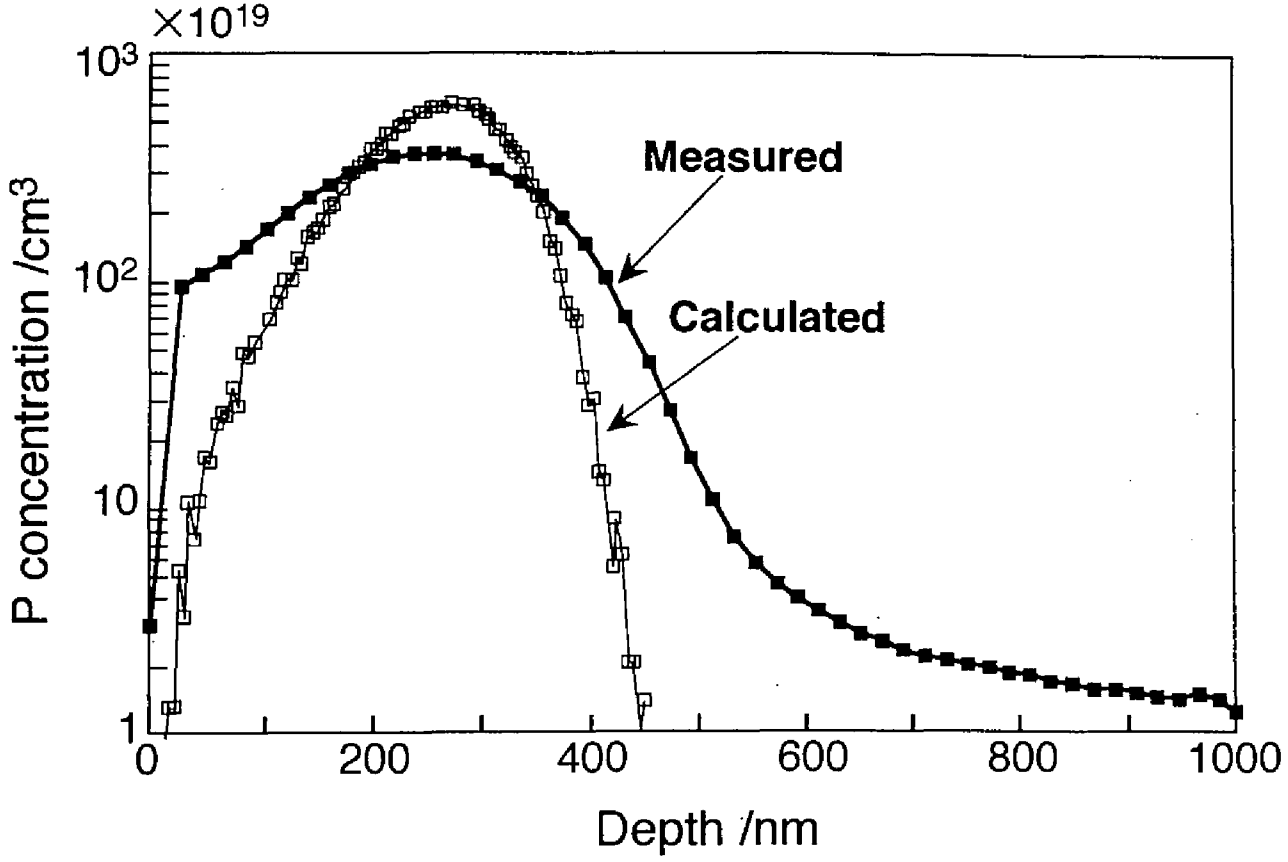

Figure 4. SIMS spectrum of the phosphorus in a silica glass plate implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}.

concentration at the maximum was about 3.6×10^{22} cm^{-3}, which is close to that of red phosphorus (about 3.89×10^{22} cm^{-2}) [11].

Figure 5 shows the TEM photograph of cross section of a silica glass implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}. A large number of particles with diameters ranging from 10 to 150 nm were observed, being widely distributed at a layer centered at about 200-250 nm depth. This depth profile of phosphorus is consistent with the result of SIMS measurement (See Fig. 4). It should be, however, noted that the top surface of the glass remained almost unchanged except a small number of particles with few nm diameter.

Figure 6 shows the μRHEED pattern at a particle seen in a silica glass implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}. No remarkable ring pattern ascribed to a crystal was observed. This indicates that the implanted phosphorus is present as amorphous state.

Figure 7 shows the concentrations of the phosphorus and silicon released from the glasses implanted with P^+ ions at 200 keV with different doses into water at 95°C for 7 days. For all the doses, the glasses little released both the phosphorus and silicon.

Figure 8 shows the RBS spectra of silica glasses implanted with P^+ ions at 200 keV with different doses and soaked in water at 95°C for 7 days. It can be seen from the spectral profiles that most of the implanted phosphorus was retained in all the glasses even after the soaking.

Figure 5. TEM photograph of cross section of a silica glass plate implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}. *: Spot for μRHEED analysis (See Fig. 6).

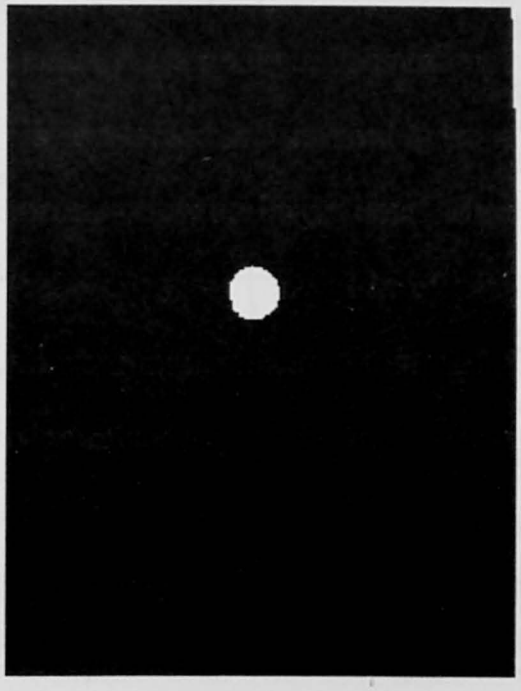

Figure 6. μRHEED pattern at a particle seen in a silica glass plate implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}.

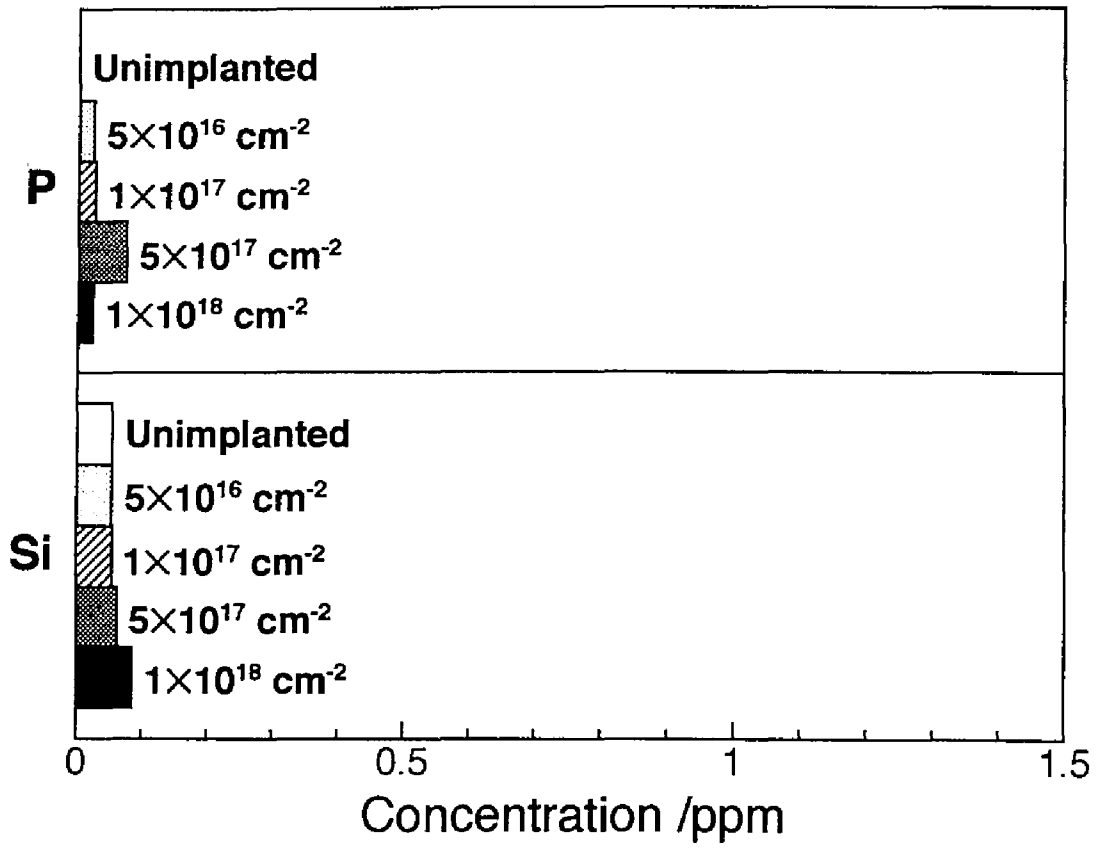

Figure 7. Concentrations of P and Si released from silica glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2} and soaked in water at 95°C for 7 days.

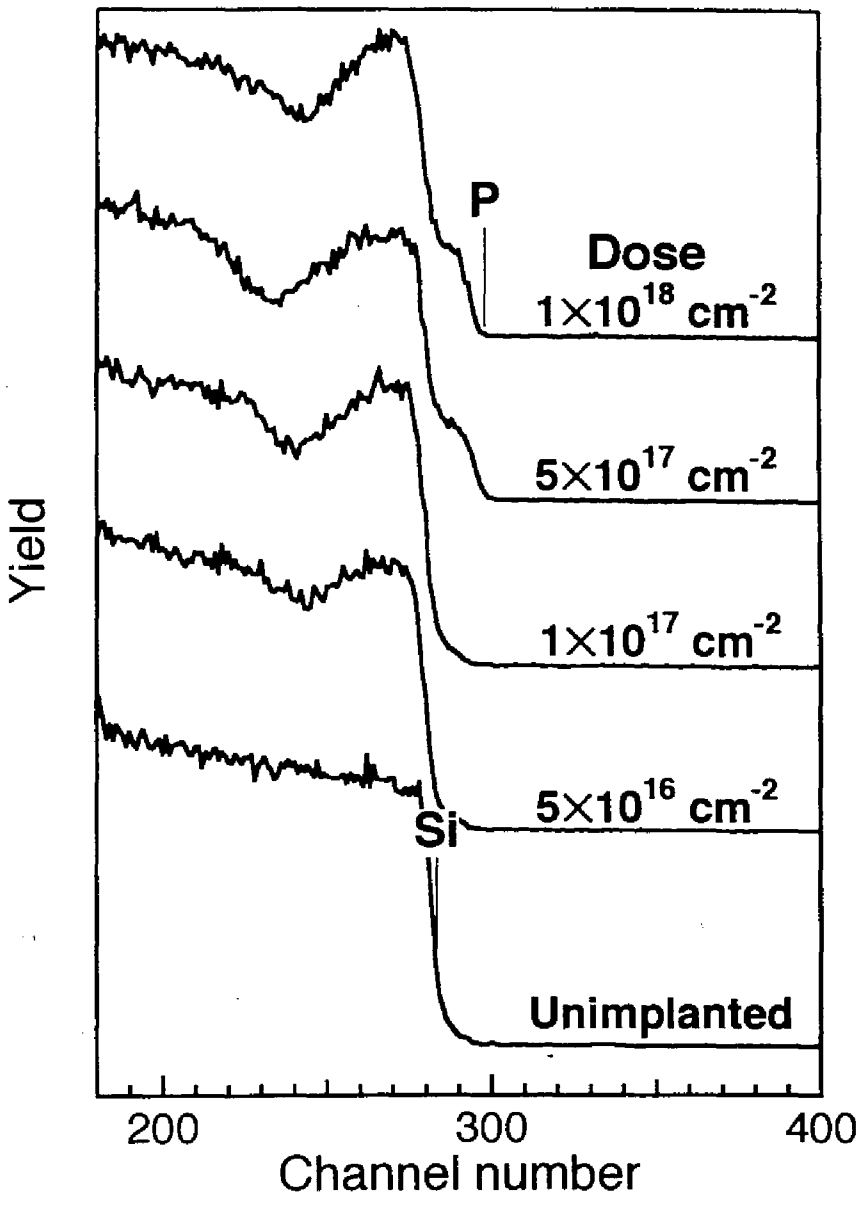

Figure 8. RBS spectra of silica glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2} and soaked in water at 95°C for 7 days.

4. Discussion

The amount of the phosphorus ion implanted into the silica glass was not saturated even to a dose of 1×10^{18} cm^{-2} at 200 keV, while that was saturated at 5×10^{16} cm^{-2} for 20 keV, and 5×10^{17} cm^{-2} for 50 and 100 keV in the Chapters 1-3. These results indicate that a large amount of phosphorus can be incorporated into a silica glass by ion implantation at an energy as high as 200 keV. This is explained by assuming that the maximum concentration of the phosphorus exists at a larger depth from the surface of the silica glass in 200 keV than in 20, 50 and 100 keV; i.e. the maximum concentrations of the phosphorus implanted at 20, 50, 100 and 200 keV are theoretically estimated to be located at 19.9, 48.6, 100.2 and 207.3 nm, respectively, in depth [7].

As shown in Fig. 2, the peak at 1150 cm^{-1} of the silica glass shifted to a lower wavenumber by the P^+ ion implantation. This shift is attributed to the formation of structural damage represented as a decrease in Si-O-Si bond angle at the surface of the glass [10, 12].

For all the doses at 200 keV, since the phosphorus ion was scarcely distributed up to the surface (See Fig. 3), no phosphorus was oxidized at the surface of the glass by atmospheric oxygen. On the other hand, the phosphorus ion was distributed up to the surface of the glass to be oxidized even for the doses of 5×10^{16}, 1×10^{17} and 5×10^{17} cm^{-2} at 20, 50 and 100 keV, respectively, as shown in Chapters 1-3. The latter results indicate that the

implanted phosphorus reaches the glass surface and then reacts with atmospheric oxygen when its amount is close to the saturated one for each implantation energy.

The SIMS spectrum in Fig. 4 indicates that the phosphorus ions are widely distributed in a layer centered at 200-250 nm depth. This spectrum suggests that the implanted phosphorus ions diffused inward and outward during the ion implantation because the phosphorus concentration at the maximum was so high as to be close to that in red phosphorus. As a result, the broad band, where a lot of the implanted phosphorus exists, was formed by the P^+ ion implantation.

It can be seen from TEM image (See Fig. 5) that many particles with diameters ranging from 10 to 150 nm are formed and widely distributed in a layer centered at 200-250 nm depth by the P^+ ion implantation at 200 keV with a dose of 1×10^{18} cm^{-2}, but they scarcely distributed to the top surface of glass. The μRHEED pattern at a particle seen in the silica glass indicates that these particles are amorphous (See Fig. 6). Taking into also account that the silica glass was colored brown by the P^+ ion implantation, it is concluded that the implanted phosphorus ions form amorphous phosphorus colloid particles [13] in the glass.

The silica glasses which were implanted with the P^+ ions at 200 keV with doses from 5×10^{16} to 1×10^{18} cm^{-2} hardly released both the phosphorus and silicon. The little amount of phosphorus released from these glasses is attributed to almost no presence of the phosphorus at the surface of the

glass as discussed above. The release of the silicon from these glasses is as little as that from the unimplanted silica glass (See Fig. 7). This means that the structural damage of the silica glass, which was formed by the ion implantation, had no adverse effect on the chemical durability of the silica glass even at a high acceleration energy of 200 keV, similar to 20, 50 and 100 keV.

As shown in Chapters 1-3, at 20, 50 and 100 keV, even the silica glasses implanted with doses as low as 5×10^{16}, 1×10^{17} and 5×10^{17} cm^{-2}, respectively, released appreciable amounts of the phosphorus and silicon. This is attributed to the presence of the phosphorus oxide, which is known to be hygroscopic [11], at the surfaces of these glasses. This is in contrast with the present results at 200 keV where little phosphorus was distributed up to the glass surface even with a high dose of 1×10^{18} cm^{-2}.

The number of the phosphorus ion present in one microsphere of 20 μm in diameter of the silica glass implanted with P^+ ion with a dose of 1×10^{18} cm^{-2}, is 2.09×10^{-12} mol. This numbers are a little smaller than that (4.88×10^{-11} mol) of yttrium ion present in one microsphere in the same size of the glass of the composition $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%), which is already clinically used for the radiotherapy. The silica glass implanted with P^+ ions even with a dose of 1×10^{18} cm^{-2} could, however, give large irradiation of short-ranged highly ionizing β-ray to the tumors comparably to the $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass, since a half-life of ^{32}P (14.3 d) is about five times as long as that of ^{90}Y (64.1 h).

On the other hand, the number of the phosphorus ion released from the silica glass, implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}, into the hot water is 7.89×10^{-9} $mol\cdot cm^{-2}$. Since this value is less than the number of the yttrium, 3.04×10^{-8} $mol\cdot cm^{-2}$, released from $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass into the same hot water, which was measured by the present authors, this glass can be said to show sufficiently high chemical durability to be used for *in situ* irradiation of cancer.

In conclusion, a radiotherapy glass, with not only with high phosphorus content but also with high chemical durability, can be obtained, when the P^+ ion is implanted into a silica glass at 200 keV with a dose of 1×10^{18} cm^{-2}.

5. Summary

In this chapter, acceleration energy of P^+ ion implantation was furthermore elevated up to 200 keV, which is the highest energy available with the popular ion implanter commercialized. The amount of phosphorus in the glass was not saturated even at a high dose of 1×10^{18} cm^{-2} under this acceleration energy. Nearly all the implanted phosphorus was present not in the surface region but in the inner region of the glass, taking a form of phosphorus colloid for all the doses in the range from 5×10^{16} to 1×10^{18} cm^{-2}. It was observed that the implanted phosphorus

formed amorphous phosphorus colloid particles in diameters ranging from 10 to 150 nm, being distributed widely in a layer centered at 200-250 nm depth, in the silica glass implanted with a dose of 1×10^{18} cm^{-2}. The silica glass implanted even with a high dose such as 1×10^{18} cm^{-2} hardly released both of the phosphorus and silicon into water at 95°C for 7 days. This is in contrast with the results for implantation energies of 20, 50 and 100 keV, where even doses of 5×10^{16}, 1×10^{17} and 5×10^{17} cm^{-2}, respectively, gave the oxidized phosphorus on the glass surfaces and appreciable releases of the phosphorus and silicon into the hot water. This indicates that a chemically durable silica glass containing the phosphorus in the amount comparable to the yttrium in the Y_2O_3-Al_2O_3-SiO_2 glass can be obtained, when P^+ ion is implanted at a high energy to be localized in a deep region from the glass surface without forming chemically less durable oxidized phosphorus at the glass surface, even if the surface structure is damaged by the ion implantation.

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CHAPTER 5

STRUCTURE AND PROPERTIES OF SILICA GLASS MICROSPHERES IMPLANTED WITH P^+ IONS

1. Introduction

Radiotherapy is one of the effective for cancer treatments without excising the host organ. Irradiation is, however, generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it has been reported that a glass microsphere of 20 to 30 μm in diameter of $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition is useful for *in situ* irradiation of cancers [1-4]. Yttrium-89 (100% natural abundance), ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) in this glass can be activated to β-emitters of ^{90}Y, ^{28}Al and ^{31}Si with half-lives of 64.1 h, 2.25 min. and 2.62 h by neutron bombardment, respectively [5]. Other silicons and oxygen are not activated by the neutron bombardment. The radioactivity of this glass, however, may remarkably decreased even before the cancer treatment, because even ^{90}Y has a short half-life of 64.1 h [5].

A chemically durable glass microspheres containing a large amount of phosphorus are believed to be useful for *in situ* radiotherapy of deeply seated cancers, since ^{31}P in this glass can be activated to β-emitter ^{32}P with a half-life of 14.3 days by neutron bombardment [5]. Such phosphorus-containing glass microspheres with high chemical durability are expected to be prepared by phosphorus ion implantation into a silica glass microspheres.

In Chapters 1-4, phosphorus ion implantation under different acceleration energies into a pure silica glass plate was attempted in order to reveal the condition for preparing a chemically durable glass containing the phosphorus in high concentration. The studies in the previous chapters showed that such glass can be obtained if the phosphorus (P^+) ions are implanted into the silica glass at a higher energy to be localized in a deep region.

In this chapter, phosphorus ion implantation was applied to silica glass microspheres 20 to 30 μm in diameter, which can be used in a practical *in situ* radiotherapy, at 50 keV with different doses. The surface structural change and chemical durability of the glass microsphere were investigated in comparison with those of P^+-implanted silica glass plates described in the previous chapters. Based on these results, the implantation method adequate for phosphorus ion implantation into glass microspheres was discussed.

2. Experimental

2.1. P^+ Ion Implantation into Silica Glass Microspheres

Highly pure silica glass microspheres of 25 μm in average diameter (metallic impurities< 300 ppm) was prepared by flame spherodization (HARIMIC SW-CO5, Maikuron Corp., Himeji, Japan). Phosphorus ion (P^+) was produced by thermoelectron bombardment to red phosphorus vapor, and implanted into the glass microspheres at 50 keV with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2} by an ion implanter (NH-20SR, Nissin Electrical Co. Ltd., Tokyo, Japan). As shown in Figure 1, the glass microspheres of 5.0 g were put into a stainless container 30 mm×40 mm×20 mm in size on a vibrator, and this container was continuously vibrated with a frequency of 200 Hz during the ion implantation so that P^+ ion was implanted into them uniformly. A secondary-electron shower was irradiated to the microspheres to reduce charge-up at their surfaces. The low mean current density (100-400 $\mu A\cdot cm^{-2}$) was used for preventing a remarkable temperature increase of the glass microspheres during the ion implantation.

2.2. Analysis of Glass Microsphere Surface

The depth profile of phosphorus was measured with three dimensional secondary ion mass spectroscopy (3D-SIMS) (SIMS4000, Atomica Analysetechnik GMBH, München, Germany). The ^{31}P (100%

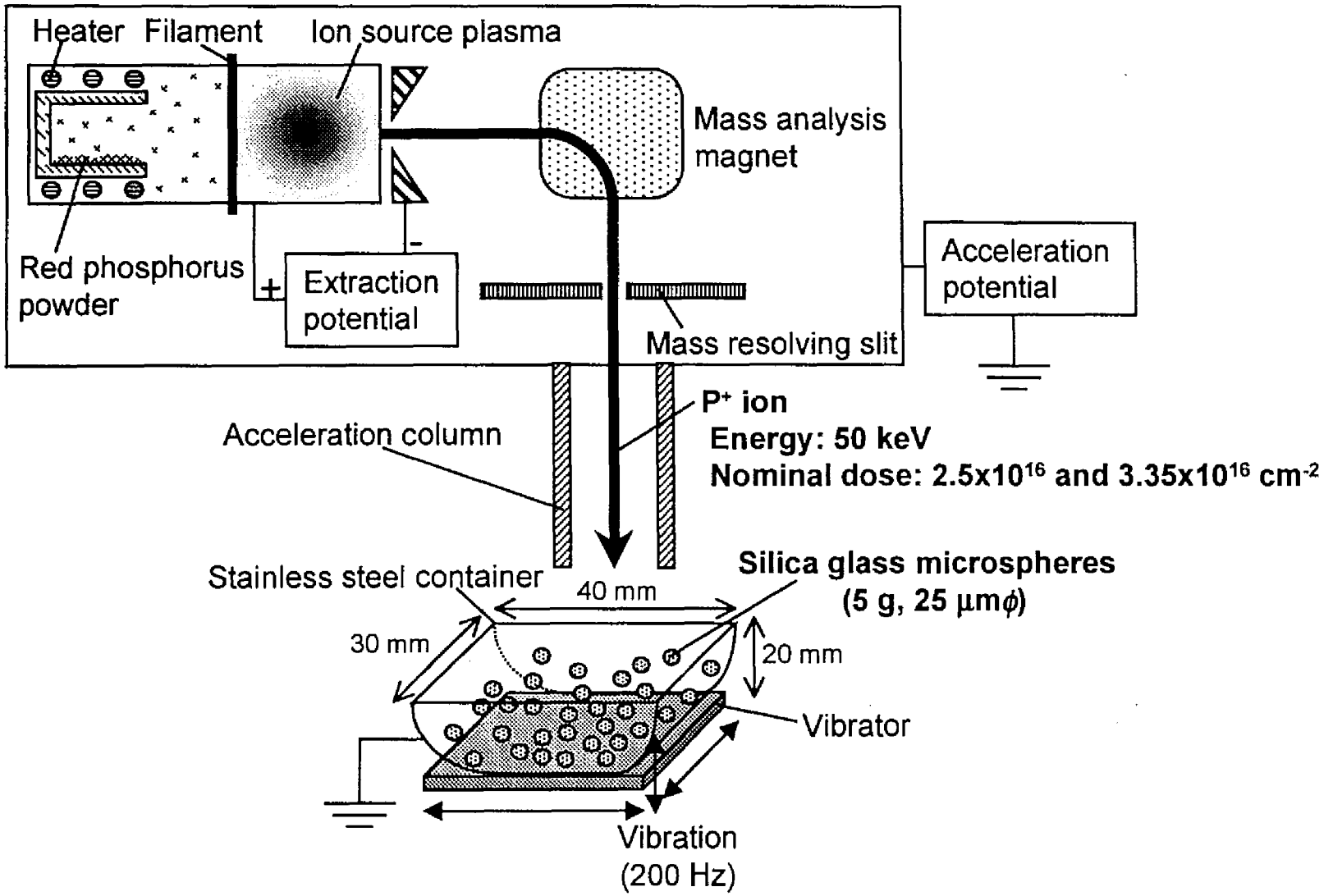

Figure 1. Schematic representation of P^+ ion implantation into silica glass microspheres.

natural abundance) and ^{18}O (20.4% natural abundance) signals were detected by Cs^+ primary beam with 0.5 μmϕ at 10 keV-100 nA. For each measurement point up to 0.3 μm depth, a 300 μm×300 μm square area was resolved into 256×256 mesh points. The intensity of ^{31}P signal was normalized by being divided that of ^{18}O signal in the silica glass matrix.

The chemical state of elements in the glass microspheres were investigated by measuring survey spectrum with X-ray photoelectron spectroscopy (XPS) (MT-5500, ULVAC-PHI Co. Ltd., Chigasaki, Japan). MgKα (1253.6 eV) X-ray was used as an excitation source at the residual pressure of 10^{-9} Pa. The photoelectron take-off angle (the angle between the sample surface and the detector axis) was set at 45°. The measured binding energies were corrected with reference to the binding energy of C_{1s} (284.6 eV) of the hydrocarbon adsorbed on the sample surfaces.

Surface structures of the glass microspheres was analyzed with Fourier transform infrared diffusive reflection spectroscopy (FT-IR 5M, JASCO, Tokyo, Japan) with a 45° incident angle. For the FT-IR diffusive reflection spectroscopic measurement, the glass microspheres were pulverized, and mixed homogeneously with powdered KBr at a sample to KBr ratio of 1:100.

2.3. Chemical Durability Test

The P^+-implanted glass microspheres of 0.20 g were immersed in 20 ml of distilled water at 95°C in a polypropylene bottle, shaken at a rate of

120 strokes·min^{-1} with a stroke length of 3 cm. After 7 days, the concentrations of the phosphorus and silicon, released from the glass microspheres into the hot water, were measured with inductively coupled plasma (ICP) atomic emission spectroscopy (SPS-1500VR, Seiko Instruments Inc., Tokyo, Japan).

3. Results

Figure 2 shows the 3D-SIMS image of silica glass microspheres, which were implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2}, at 25 nm depth. It can be seen from this figure that P^+ ions were successfully implanted into silica glass microspheres by the present method. The intensity of phosphorus SIMS signal was relatively larger in center than in periphery of microsphere, since the sputtering yield in the SIMS measurement was higher in center than in periphery of microsphere.

Figure 3 shows the depth profile of phosphorus concentration in a silica glass microsphere implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2}. The implanted phosphorus widely distributed in deep regions centered at about 50 nm depth. The maximum concentration of phosphorus was estimated at about 2.0×10^{22} cm^{-3} at about 50 nm depth. The real dose of phosphorus was calculated at 1.5×10^{17} cm^{-2} from the area

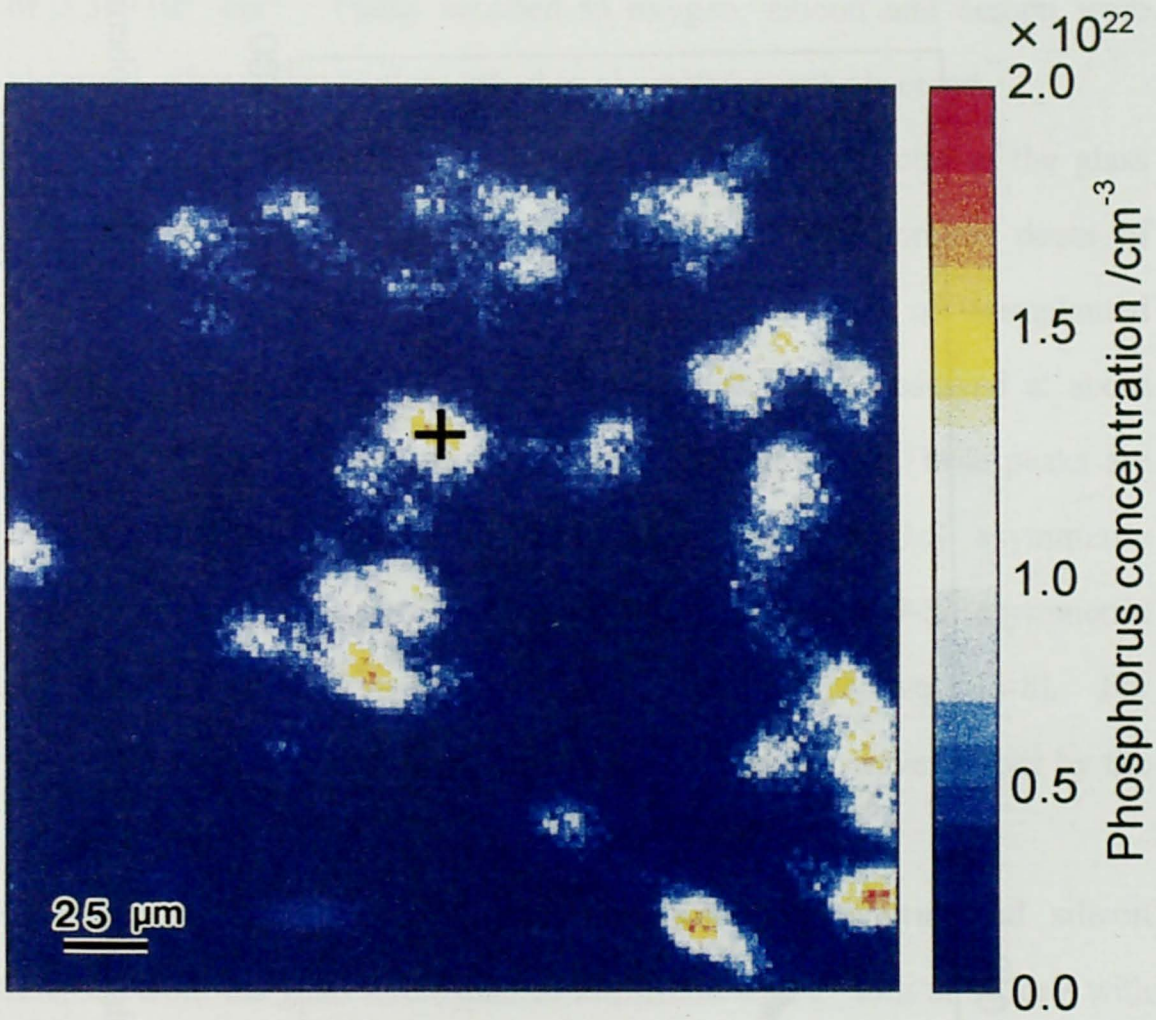

Figure 2. 3D-SIMS image of silica glass microspheres implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2} at 25 nm depth. (+: measuring point for depth profile of phosphorus concentration in Figure 3)

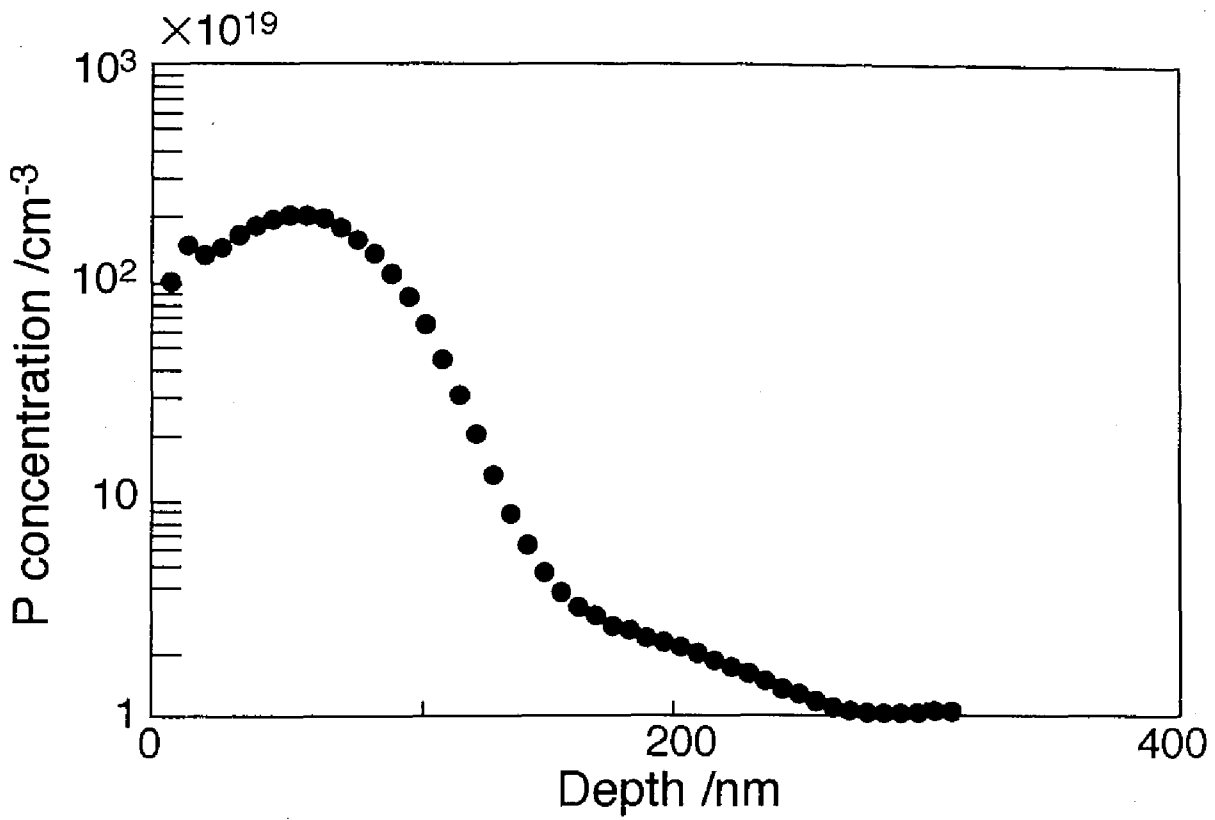

Figure 3. Depth profile of phosphorus concentration of silica glass microspheres implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2}.

of phosphorus concentration.

Figure 4 shows the survey XPS spectrum of the surface of silica glass microspheres implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2}. Peaks ascribed to oxygen, silicon and carbon were observed, whereas no peak ascribed to phosphorus was observed.

Figure 5 shows the FT-IR diffusive reflection spectra of the glass microspheres implanted with P^+ ions at 50 keV with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2}, in comparison with that of unimplanted original glass microspheres. Three broad peaks were observed at about 800(●), 1050 (△) and 1200 (○), for all the samples. These peaks are assigned to Si-O-Si symmetric stretching vibration, Si-O-Si asymmetric stretching vibration (transverse optical mode) and Si-O-Si asymmetric stretching vibration (longitudinal optical mode), respectively [6-8]. For both doses, the 1050 cm^{-1}-band was shifted to a lower wavenumber by the ion implantation.

Figure 6 shows the concentrations of the phosphorus and silicon released from the glass microspheres implanted with P^+ ions at 50 keV with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2} into water at 95°C for 7 days. The both glass microspheres little released both the phosphorus and silicon into hot water.

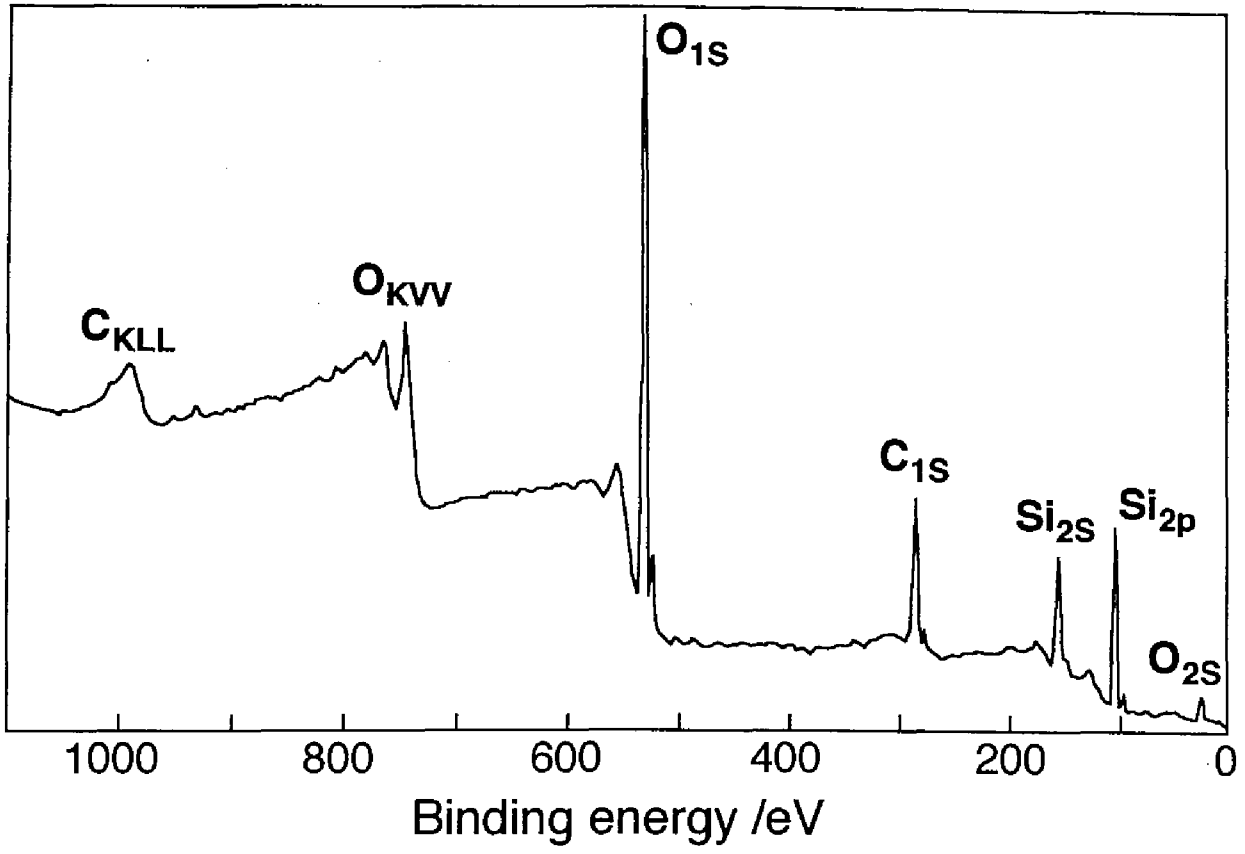

Figure 4. Survey XPS spectra of silica glass microspheres implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2}.

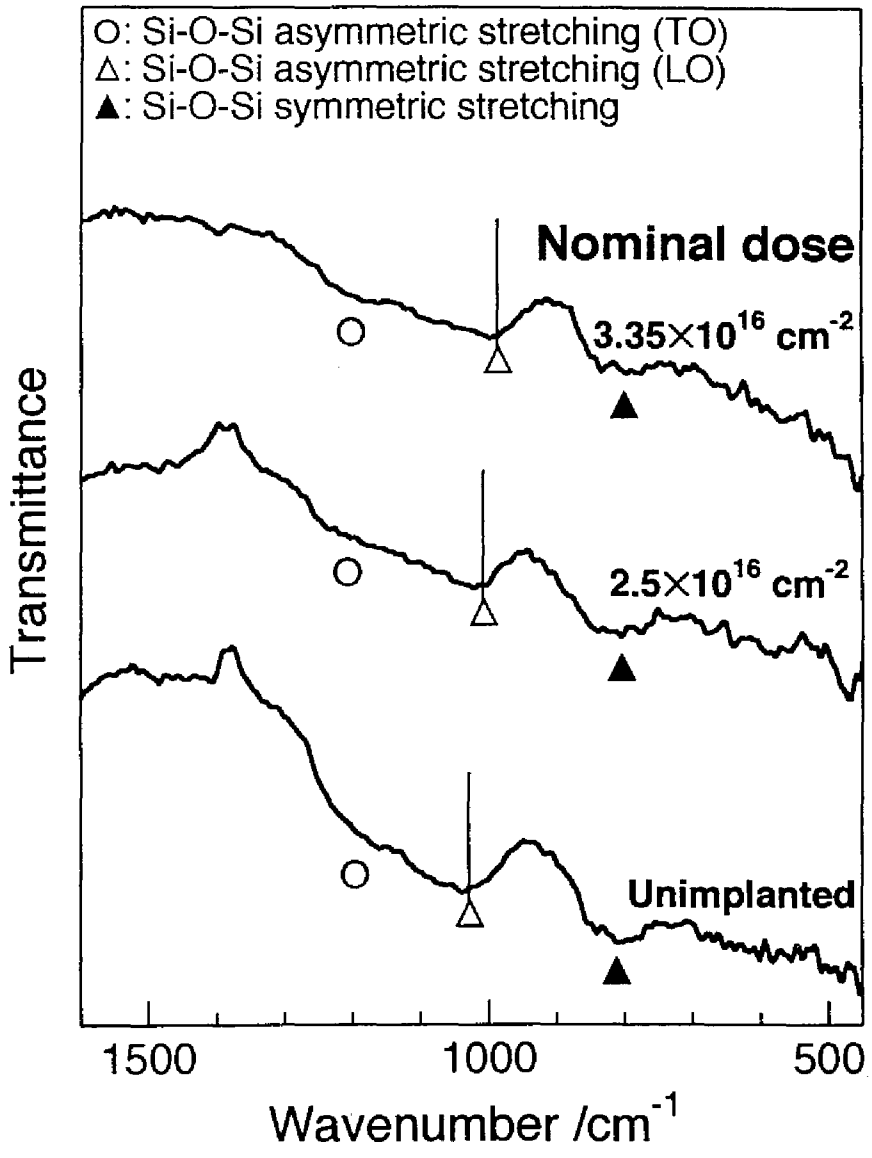

Figure 5. FT-IR diffusive reflection spectra of silica glass microspheres implanted with P^+ ions at 50 keV with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2}.

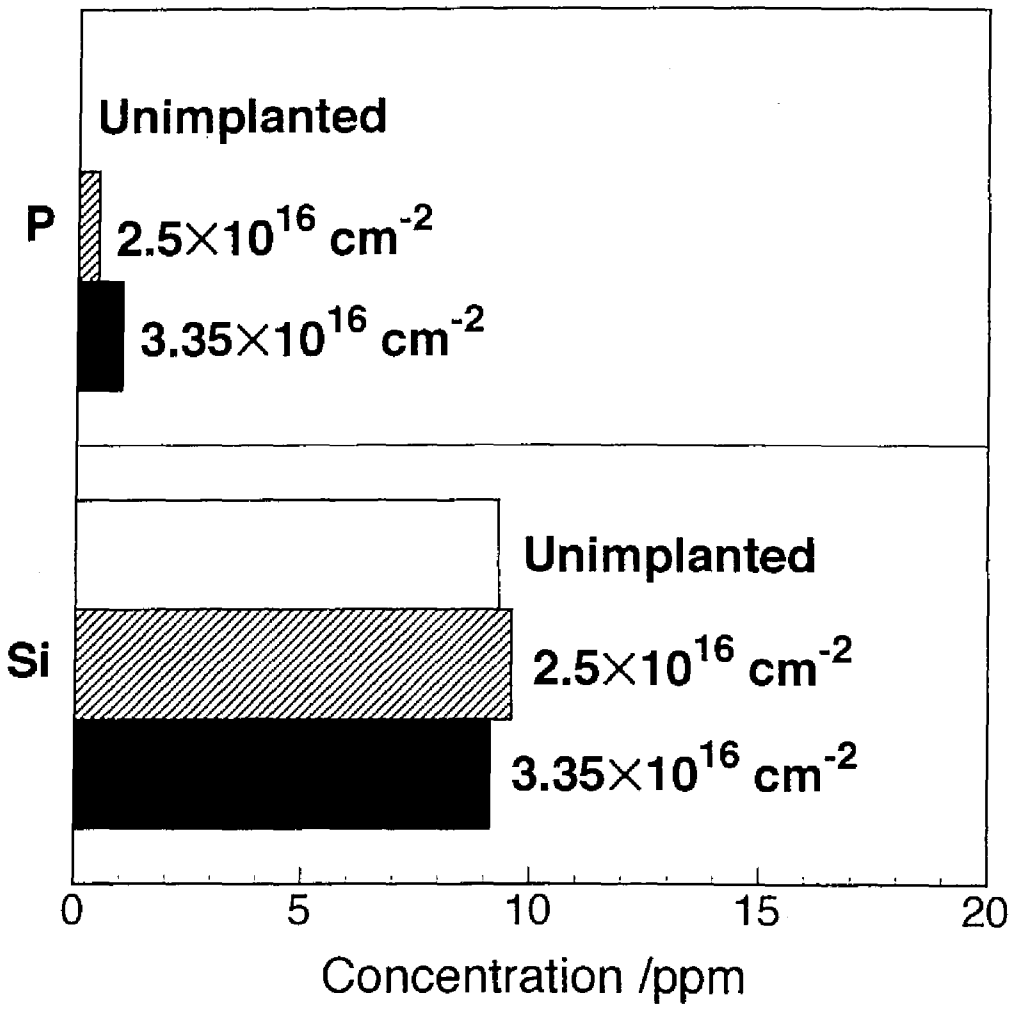

Figure 6. Concentrations of P and Si released from silica glass microspheres implanted with P^+ ions at 50 keV with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2} and then soaked in water at 95°C for 7 days.

4. Discussion

It can be seen from Figs. 2 and 3 that the phosphorus ion can be uniformly implanted to the individual microspheres by this method and that the implanted phosphorus was mainly distributed in deep regions centered at about 50 nm depth from the glass microsphere surface. It is estimated theoretically that the phosphorus implanted into the silica glass plate at 50 keV shows Gaussian distribution giving the maximum concentration at 48.6 nm in depth from the glass surface [9]. The measured maximum concentration depth (50 nm) well coincides with the calculated one (48.6 nm) in a silica glass plate. It is assumed that the penetration depth of phosphorus implanted into a silica glass microsphere is almost the same as that into a silica glass plate.

The real dose of phosphorus calculated from phosphorus concentration profile in Fig. 3 (1.5×10^{17} cm^{-2}) was about four times as large as the nominal one (3.35×10^{16} cm^{-2}). This phenomenon can be explained as follows. The nominal dose was calculated by assuming that P^+ ions are implanted into the microspheres only at normal angle against the microsphere surfaces. In the actual ion implantation, however, it is clear that P^+ ions are also implanted at off-normal angle simultaneously. As a result, a larger amount of phosphorus was implanted into the microsphere.

In the survey XPS spectrum shown in Fig. 4, no peak ascribed to phosphorus was observed. This means that the implanted phosphorus is

mainly localized in deep region of the glass microsphere with little distributing to the glass microsphere surface. Since the glass microspheres colored brown by the ion implantation, the implanted phosphorus is present as colloids [10] in the glass microsphere, as in the previous P^+ ion-implanted silica glass plates in Chapters 1-4.

As shown in Fig. 5, the peak at 1050 cm^{-1} of the silica glass microspheres shifted to a lower wavenumber by the P^+ ion implantation. This shift is attributed to the structural damage by the ion implantation represented as a decrease in Si-O-Si bond between SiO_4 tetrahedra [8, 11] at the surface of the glass microsphere, as in the case of the silica glass plate in Chapters 1-4.

The silica glass microspheres, implanted with the P^+ ions at 50 keV with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2}, hardly released both the phosphorus and silicon (See Fig. 6). The little amount of phosphorus released from these samples is attributed to no presence of the phosphorus at the surface of the glass microsphere as discussed above. The release of silicon from these samples is as little as that from the unimplanted silica glass microspheres (See Fig. 6). This means that the structural damage, which was formed at the silica glass microsphere surfaces by the ion implantation (See Fig. 5), has no effect on the chemical durability of the silica glass microspheres, as in the case of the silica glass plate in Chapters 1-4.

The amount of the phosphorus ion released from the silica glass

microspheres implanted with P^+ ions at 50 keV with a nominal dose of 3.35×10^{16} cm^{-2} into the hot water is 2.75×10^{-9} $mol\cdot cm^{-2}$. This value is much less than the amount of the yttrium, 3.04×10^{-8} $mol\cdot cm^{-2}$, released from $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass into the same hot water, which was measured by the present authors.

On the basis of the results on P^+ ion implantation to the silica glass plates in Chapters 1-4, it is expected that silica glass microspheres containing more phosphorus which is desired for actual treatment could be obtained without losing its high chemical durability, if P^+ ion would be implanted at a higher energy by the present method.

5. Summary

In this chapter, P^+ ion implantation was attempted to apply to silica glass microspheres 20 to 30 μm in diameter, which can be used for practical *in situ* radiotherapy. The phosphorus ion was implanted to the microspheres vibrating in a stainless steel bucket with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2} at 50 keV. It was confirmed that the phosphorus ion can be uniformly implanted to the individual microspheres by this method. The implanted phosphorus was localized in deep region of the glass microsphere with the maximum concentration at about 50 nm in depth without distributing up to the surface even for a nominal dose of

3.35×10^{16} cm^{-2}. Both the samples little released both the phosphorus and silicon into water at 95°C for 7 days. In view of the results on P^+ ion implantation to the silica glass plates, it is expected that silica glass microspheres containing more phosphorus which is desired for actual treatment could be obtained without losing its high chemical durability, if P^+ ion would be implanted at a higher energy by the present method.

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CHAPTER 6

STRUCTURE AND PROPERTIES OF Y_2O_3-Al_2O_3-SiO_2 GLASS PLATES IMPLANTED WITH P^+ IONS

1. Introduction

Radiotherapy is one of the most effective treatments of cancer without excising the host organ. Irradiation is, however, generally performed externally. This does not give sufficient dose of radiation to the cancer, especially to deeply seated one, but gives severe damages to healthy tissues near the surface of the body.

Alternatively, it has been reported that a glass microsphere of 20 to 30 μm in diameter of $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition is useful for *in situ* irradiation of cancers [1-4]. Yttrium-89 (100% natural abundance), ^{27}Al (100% natural abundance) and ^{30}Si (3.10% natural abundance) in this glass can be activated to β-emitters of ^{90}Y, ^{28}Al and ^{31}Si with half-lives of 64.1 h, 2.25 min. and 2.62 h by neutron bombardment, respectively [5]. Other silicons and oxygen are not activated by the neutron bombardment. The radioactivity of this glass, however, may remarkably decreased even before the cancer treatment, because even ^{90}Y has a short half-life of 64.1 h [5]. Phosphorus-31 is also activated to β-

emitter ^{32}P by the neutron bombardment and has a little longer half-life of 14.3 days [5]. Therefore, a chemically durable glass containing a large amount of phosphorus is believed to be useful for *in situ* radiotherapy of deeply seated cancers. Phosphorus-rich glasses prepared by the conventional melt-quenching method are, however, usually less chemically durable [6].

In Chapter 4, it was shown that a chemically durable silica glass with high phosphorus content can be obtained, when P^+ ion is implanted at high energy such as 200 keV to be localized in deeper region from the glass surface even if the surface structure is damaged by the ion implantation.

In this chapter, on the basis of the above results on P^+ ion implantation into silica glass plates, P^+ ion implantation was extended to Y_2O_3-Al_2O_3-SiO_2 glass plates, which is already in clinical use, at 200 keV with various doses, in order to enhance the radiotherapeutic effect of the glass. The surface structure and chemical durability of the glass was also compared with those of 200 keV implantation into silica glass plates in Chapter 4 in order to clarify the effect of the glass composition on the reaction of the implanted ion with the substrate, and the enhancement in radiotherapeutic effect by the P^+ ion implantation into Y_2O_3-Al_2O_3-SiO_2 glass was estimated.

2. Experimental

2.1. Preparation of Y_2O_3-Al_2O_3-SiO_2 Glass Plates

A powder mixture corresponding to $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) composition was prepared from reagent-grade chemicals of Y_2O_3, Al_2O_3 and SiO_2. It was melted in a platinum crucible at 1600°C for 2 h, poured on a stainless steel plate and pressed by another plate to be formed into plates about 1 mm thick. The obtained glass was cut into rectangular specimens 10 mm×10 mm×1 mm in size, polished with 3-4 μm diamond paste, washed with acetone in an ultrasonic cleaner. The glass was annealed at 850°C for 1 h in order to eliminate the strains.

2.2. P^+ Ion Implantation into Y_2O_3-Al_2O_3-SiO_2 Glass Plates

Phosphorus ion (P^+) was produced by thermoelectron bombardment to red phosphorus vapor, and implanted into the glass at 200 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2} by an ion implanter (NH-40SR, Nissin Electrical Co. Ltd., Tokyo, Japan). The P^+ ions was implanted intermittently into the samples which were scanned back and forth behind a window of 2 cm×8 cm. The mean current density in this window was 62.5 to 125 $\mu A \cdot cm^{-2}$. The temperatures of the samples rose with the ion implantation, but did not exceed 100°C. After the ion implantation, every sample was preserved in a dry nitrogen atmosphere to avoid surface oxidation of the phosphorus.

2.3. Analysis of Y_2O_3-Al_2O_3-SiO_2 Glass Surface

The content of the phosphorus implanted into the glass was measured by a Rutherford Backscattering Spectrometer (RBS). The ion beam analyzer at Radiation Laboratory of Nuclear Engineering, Kyoto University, was used with 2 MeV $^4He^+$ ions with a 170° incident angle.

The chemical states of phosphorus and yttrium were investigated by measuring the P_{2p} and Y_{3d} binding energies with an X-ray photoelectron spectrometer (XPS) (MT-5500, ULVAC-PHI Co. Ltd., Chigasaki, Japan). MgKα (1253.6 eV) X-ray was used as an excitation source at the residual pressure of 10^{-9} Pa. The photoelectron take-off angle (the angle between the sample surface and the detector axis) was set at 45°. Xenon-ion sputtering was carried out at 4 keV to measure the depth profiles. The measured binding energies were corrected with reference to the binding energy of C_{1s} (284.6 eV) of the hydrocarbons adsorbed on the sample surfaces.

The surface structure of the glass was analyzed with a Fourier transform infrared reflection (FT-IR) spectrometer (System 2000 FT-IR, Perkin-Elmer Ltd., Buckinghamshire, England), and with a thin film X-ray diffractometer (TF-XRD) (RINT-1400, Rigaku Co., Tokyo, Japan). In the FT-IR measurement, the reflection angle was fixed at 75°. The X-ray measurement was performed at step scanning mode (0.02° step, 10 sec fixed time). In the X-ray measurement, the surface of the glass was fixed

at an angle of 1° against the incident beam.

2.4. Chemical Durability Test

The glass implanted with P^+ ions was immersed into 20 ml of distilled water at 95°C in a polypropylene bottle, and shaken at a rate of 120 strokes·min^{-1} with a stroke length of 3 cm. After 7 days, the concentrations of Si, P, Al and Y released from the glasses into the hot water, were measured by an inductively coupled plasma (ICP) atomic emission spectrometer (SPS-1500 VR, Seiko Instruments Inc., Tokyo, Japan).

3. Results

Figure 1 shows the RBS spectra of Y_2O_3-Al_2O_3-SiO_2 glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16}, 1×10^{17}, 5×10^{17} and 1×10^{18} cm^{-2}. A broad peak at 200-300 in channel number was observed for all the doses. The intensity of the broad peak increased with increasing dose up to 5×10^{17} cm^{-2}, but it decreased and the peak remarkably widened for a dose of 1×10^{18} cm^{-2}. For doses of 5×10^{17} and 1×10^{18} cm^{-2}, a rising was observed at about 400 in channel number. This indicates that yttrium ions moved toward the glass surface by the ion implantation.

Figure 2 shows the FT-IR reflection spectra of Y_2O_3-Al_2O_3-SiO_2

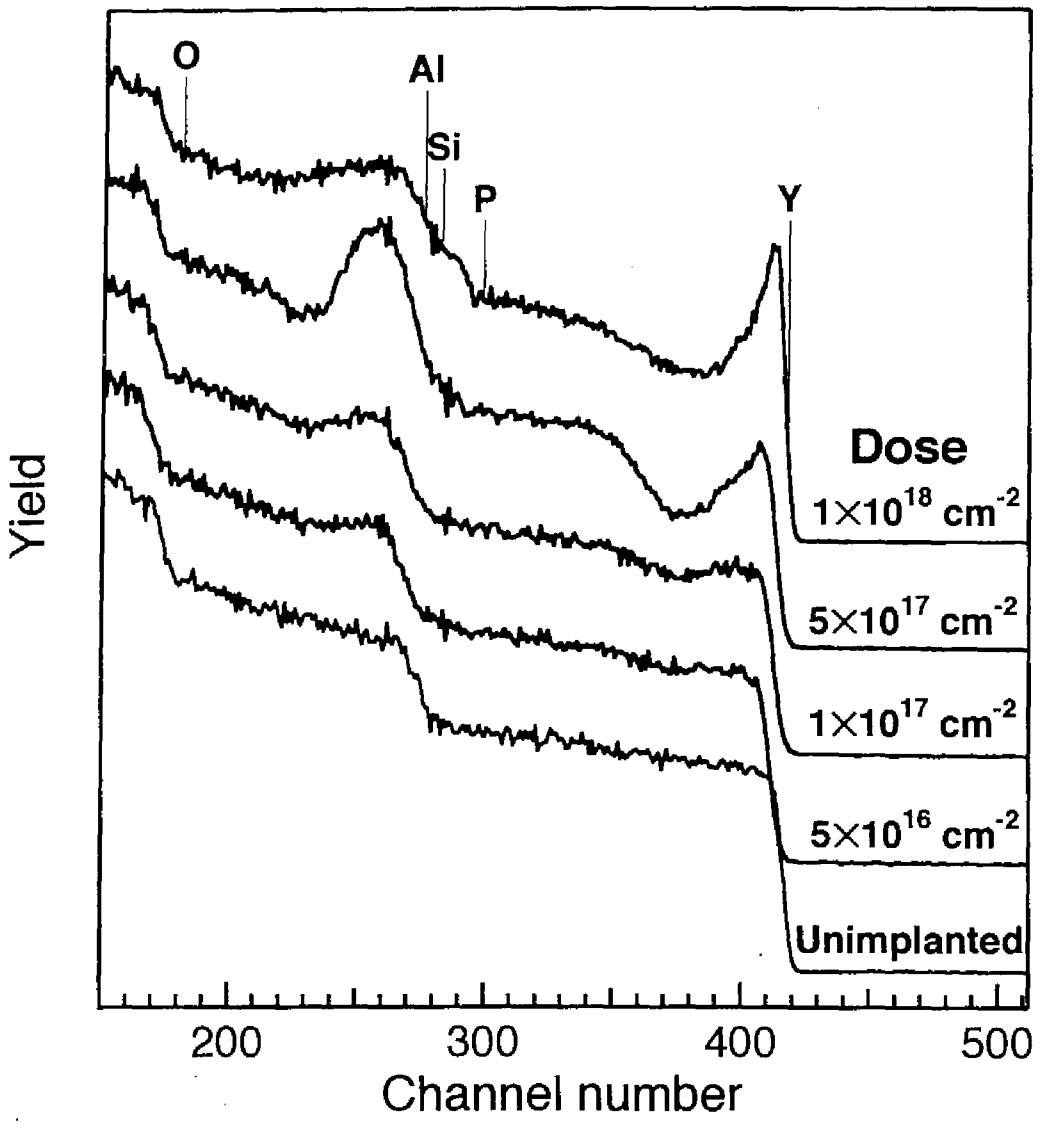

Figure 1. RBS spectra of Y_2O_3-Al_2O_3-SiO_2 glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

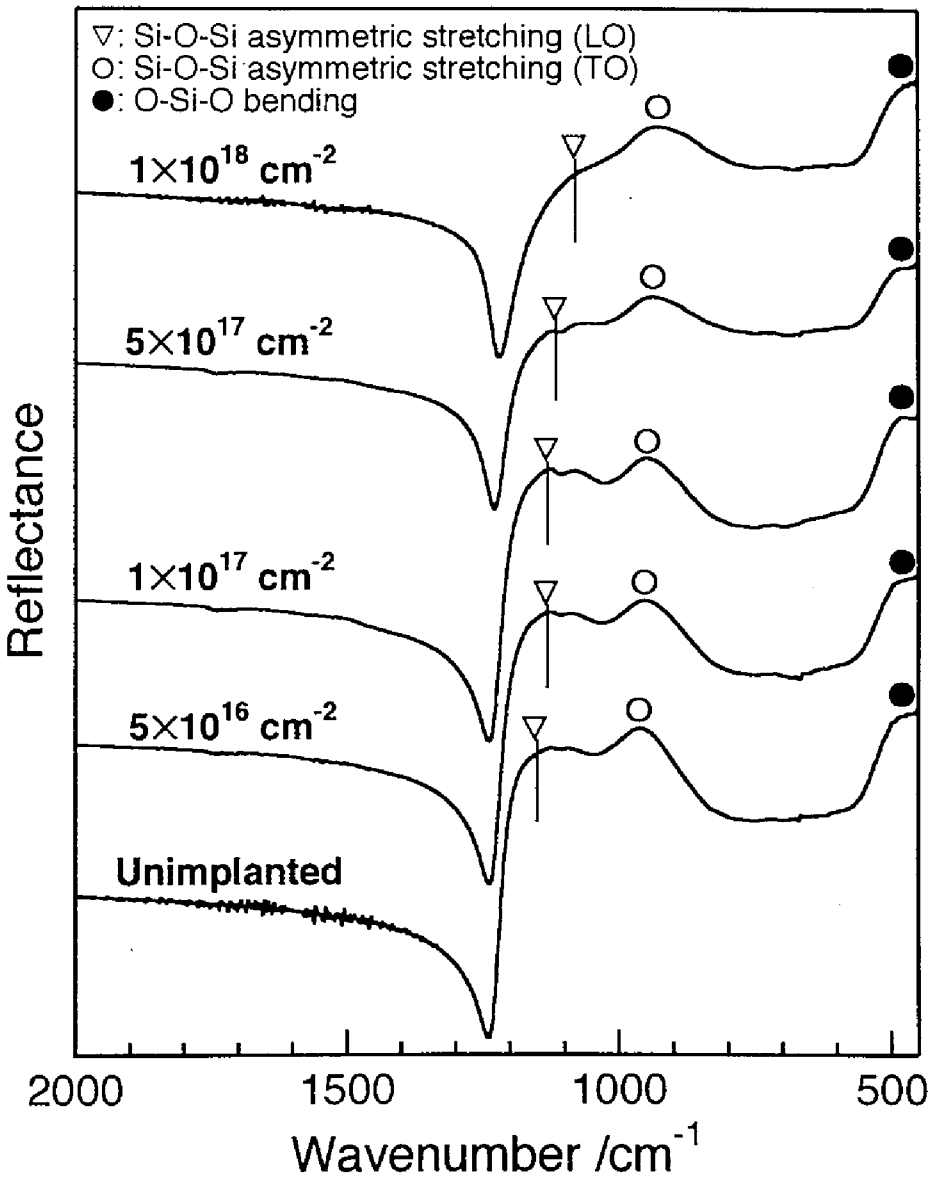

Figure 2. FT-IR reflection spectra of Y_2O_3-Al_2O_3-SiO_2 glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

glasses implanted with P^+ ions at 200 keV with various doses. Three broad peaks were observed at about 490 (●), 950 (○) and 1150 (▽) cm^{-1} for all the glasses. These peaks are assigned to O-Si-O bending vibration, Si-O-Si asymmetric stretching vibration (transverse optical mode), Si-O-Si asymmetric stretching vibration (longitudinal optical mode), respectively [7-9]. The peak at 1150 cm^{-1} was shifted to a lower wavenumber by the ion implantation, and its intensity decreased with increasing dose.

Figure 3 shows the P_{2p} XPS spectra of Y_2O_3-Al_2O_3-SiO_2 glass plates implanted with P^+ ions at 200 keV with various doses. For doses of 5×10^{16} and 1×10^{17} cm^{-2} ((a) and (b)), no peak was observed near the glass surface. For a dose of 5×10^{17} cm^{-2} ((c)), a peak was observed at 134 eV at the glass surface. For a dose of 1×10^{18} cm^{-2} ((d)), two peaks were observed at 130 and 134 eV at the glass surface. The binding energies of 130 and 134 eV are assigned to elemental phosphorus (P-P) and oxidized phosphorus (P-O), respectively. The intensity of peak ascribed to elemental phosphorus increased with increasing depth, while the peak ascribed to oxidized phosphorus disappeared in deeper regions of the glass.

Figure 4 shows the TF-XRD pattern of a Y_2O_3-Al_2O_3-SiO_2 glass plate implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}, in comparison with that of unimplanted original glass plate. Five small broad peaks (indicated by ▼) were observed at about 12, 15, 27, 32 and 45° in 2θ for P^+-implanted Y_2O_3-Al_2O_3-SiO_2 glass. Although none of these peaks is assigned to any known crystalline phase, it is found from this

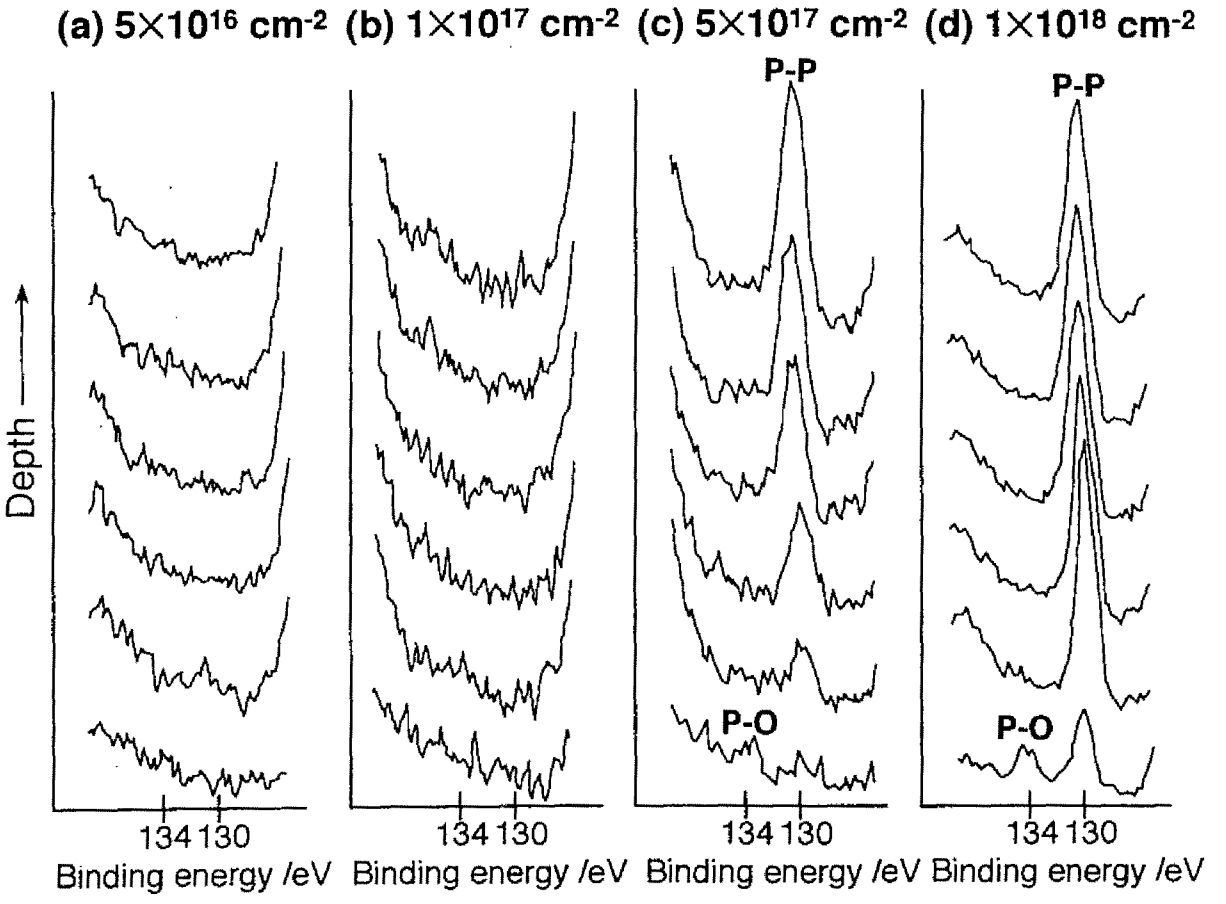

Figure 3. P_{2p} XPS spectra of Y_2O_3-Al_2O_3-SiO_2 glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}.

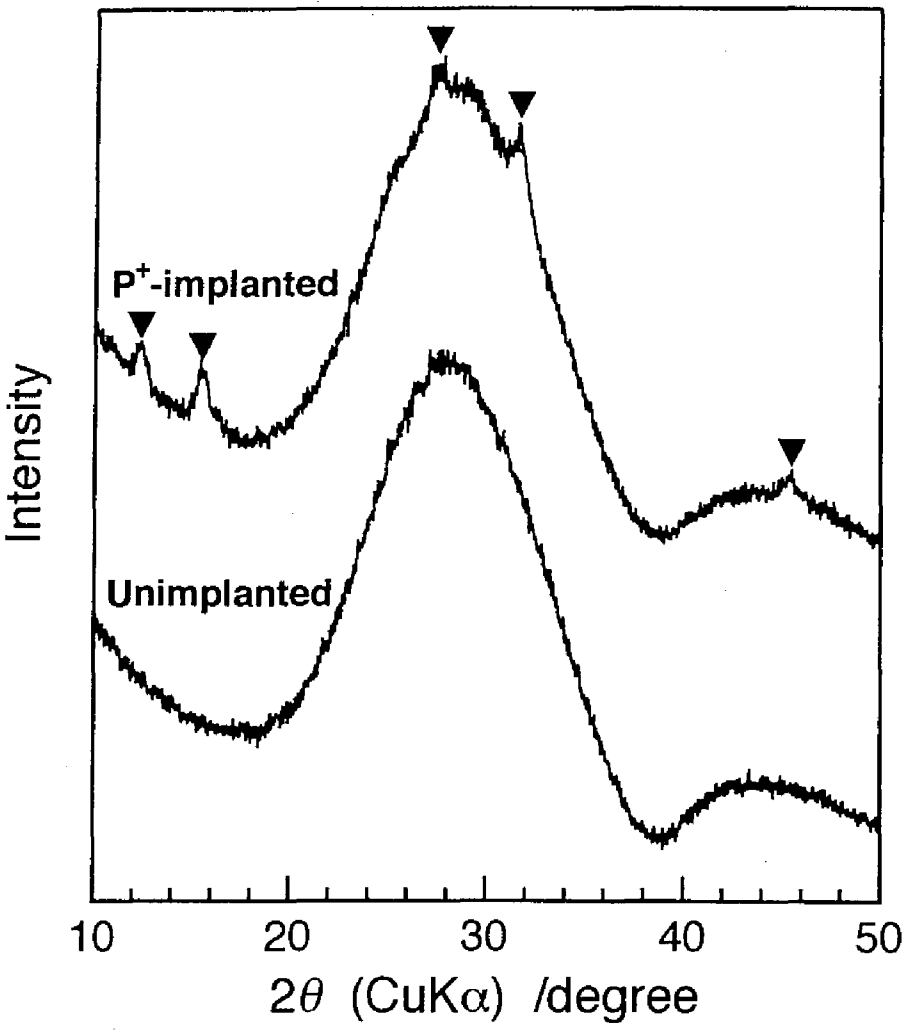

Figure 4. TF-XRD pattern of a Y_2O_3-Al_2O_3-SiO_2 glass plate implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}, in comaprison with that of unimplanted original glass plate.

pattern that a small amount of certain fine crystal was precipitated at the glass surface by the ion implantation.

Figure 5 shows the Y_{3d} XPS spectrum of Y_2O_3-Al_2O_3-SiO_2 glass implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}, in comparison with that of unimplanted original glass. Two large peaks were observed at 157.5 and 159.5 eV for both specimens. These peaks are assigned to Y-O bond in glassy Y_2O_3 [10]. A shoulder (indicated by ↓) was observed at about 155.5 eV for P^+-implanted Y_2O_3-Al_2O_3-SiO_2 glass. This result indicates that a small amount of yttrium which has a different binding state from yttrium in glassy Y_2O_3 existed at the surface of P^+-implanted Y_2O_3-Al_2O_3-SiO_2 glass.

Figure 6 shows the concentrations of Si, P, Al and Y released from Y_2O_3-Al_2O_3-SiO_2 glasses implanted with P^+ ions at 200 keV with various doses into water at 95°C for 7 days. The glasses implanted with doses of 5×10^{16} and 1×10^{17} cm^{-2} released little amounts of Si, P, Al and Y into the hot water, while the glasses implanted with doses above 5×10^{17} cm^{-2} did appreciable amounts of these elements under the same condition.

Figure 7 shows the RBS spectra of Y_2O_3-Al_2O_3-SiO_2 glasses implanted with P^+ ions at 200 keV with various doses and then soaked in water at 95°C for 7 days. A broad peak at 200 to 300 in channel number disappeared after the soaking for all the investigated doses, and a rising at about 400 in channel number also disappeared after the soaking for doses above 5×10^{17} cm^{-2}.

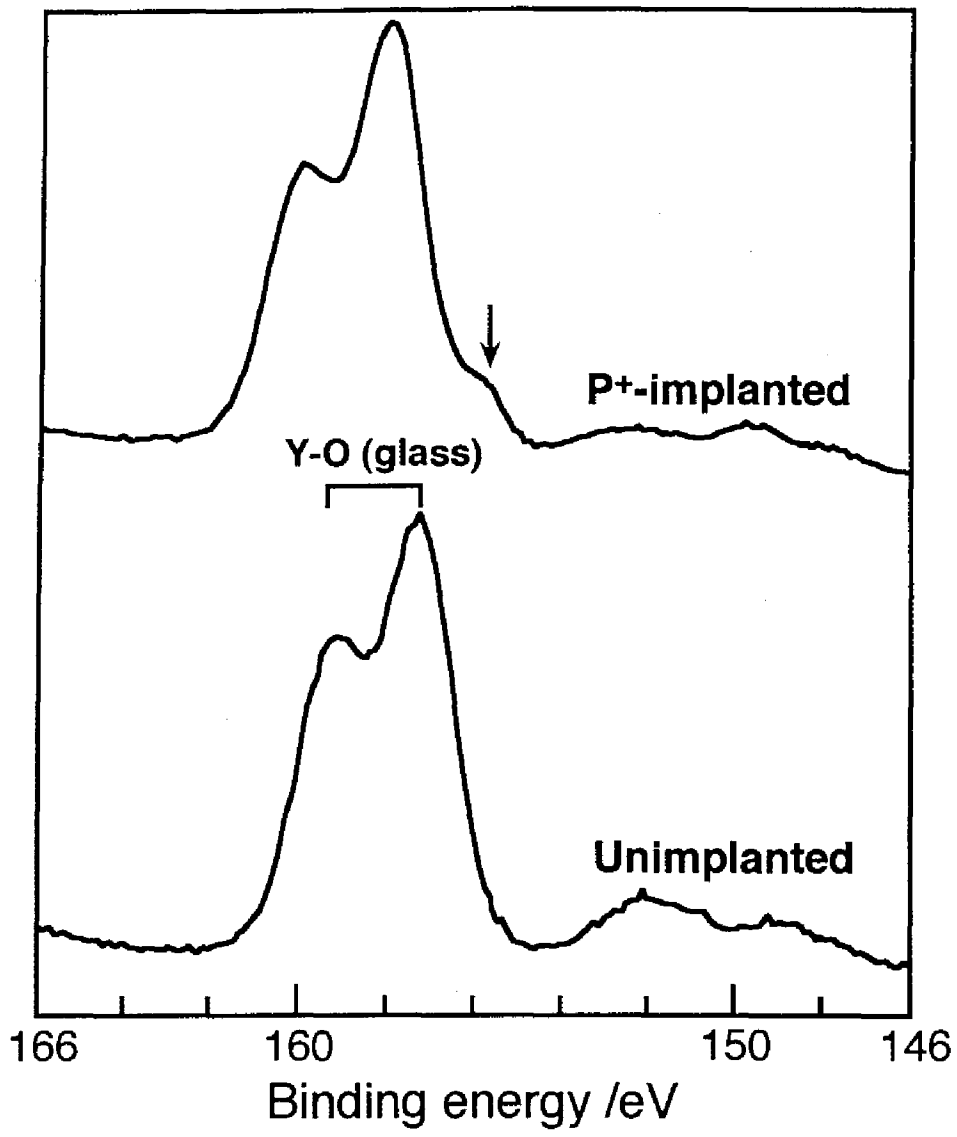

Figure 5. Y_{3d} XPS spectrum of a Y_2O_3-Al_2O_3-SiO_2 glass plate implanted with P^+ ions at 200 keV with a dose of 1×10^{18} cm^{-2}, in comparison with that of unimplanted original glass plate.

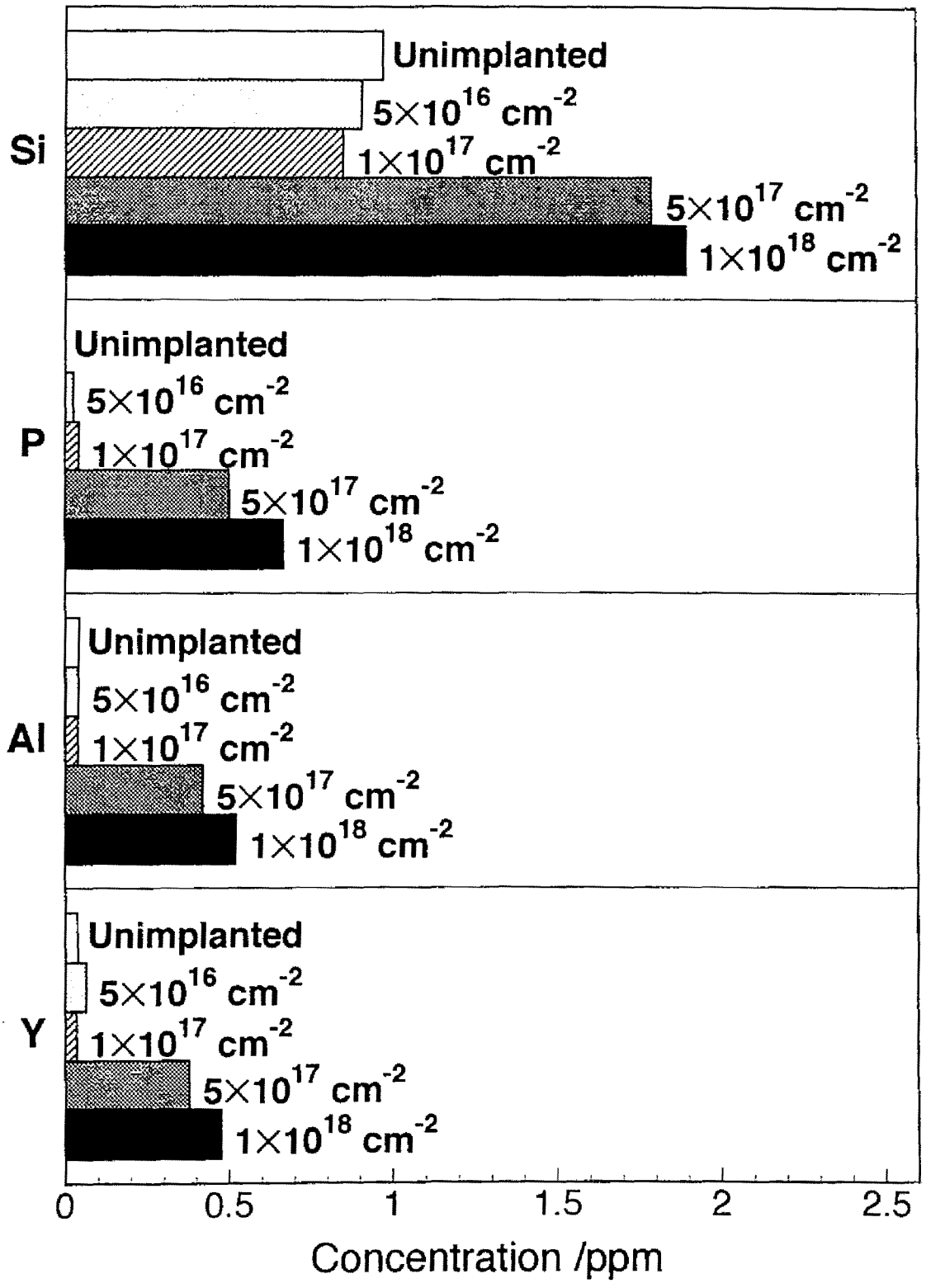

Figure 6. Concentrations of elements released from Y_2O_3-Al_2O_3-SiO_2 glass plates implanted with P^+ ions at 200 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2} into water at 95°C for 7 days.

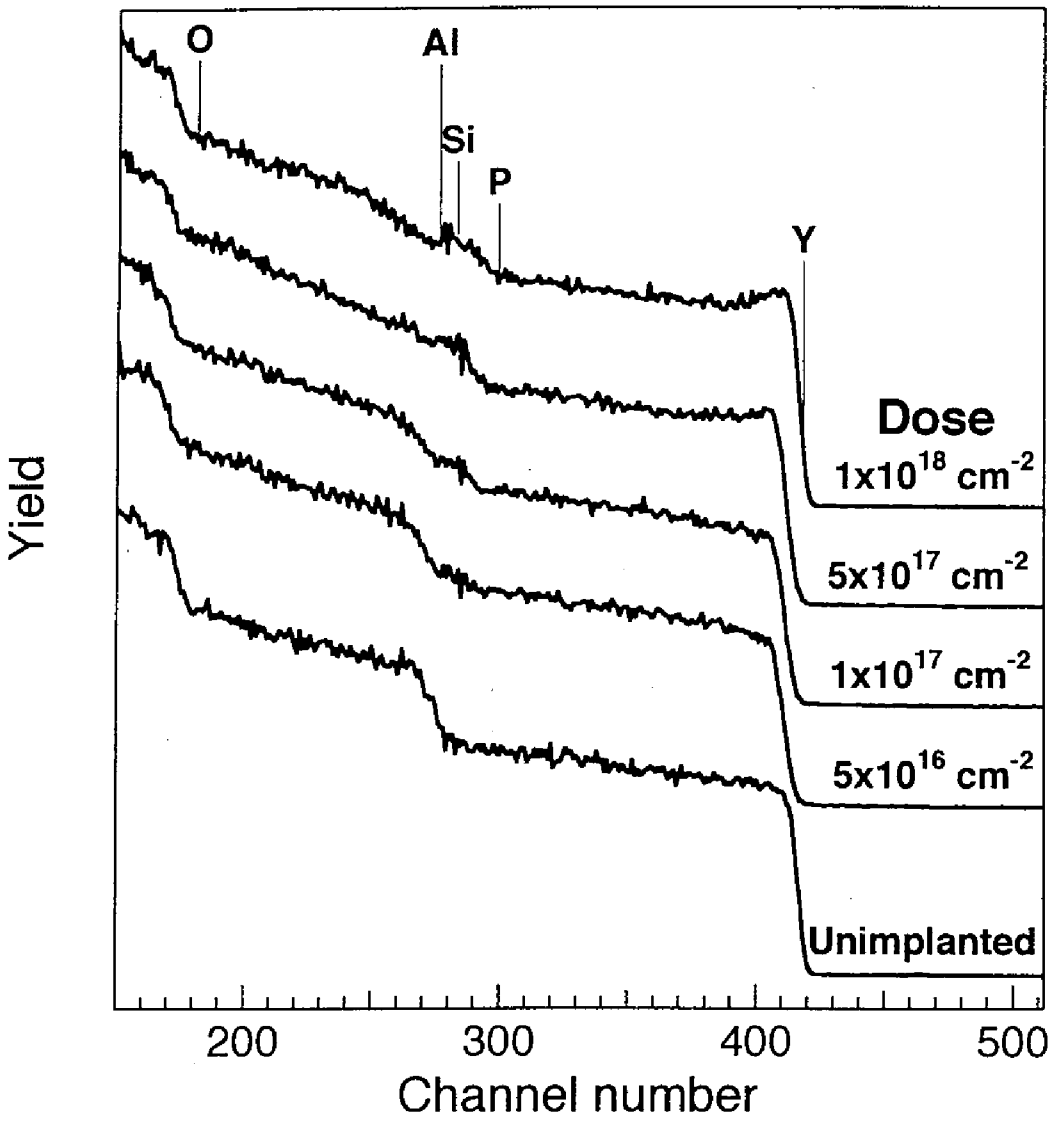

Figure 7. RBS spectra of Y_2O_3-Al_2O_3-SiO_2 glasses implanted with P^+ ions at 200 keV with different doses and then soaked in water at 95°C for 7 days.

4. Discussion

The peak at 200-300 in channel number on RBS spectrum remarkably widened for a dose of 1×10^{18} cm^{-2} as shown in Fig. 1. It is assumed from this result that the implanted phosphorus ions diffused inward and outward during the ion implantation because the phosphorus concentration at the maximum was so high for a dose of 1×10^{18} cm^{-2}. Therefore, the amount of the phosphorus ion might be nearly saturated at a dose of 5×10^{17} cm^{-2} at 200 keV for Y_2O_3-Al_2O_3-SiO_2 glass. On the contrary, it was not saturated even with a dose of 1×10^{18} cm^{-2} at the same acceleration energy for silica (SiO_2) glass as shown in Chapter 4. These phenomena can be explained as follows. A maximum concentration depth of the implanted phosphorus is shallower in Y_2O_3-Al_2O_3-SiO_2 glass than in silica glass, since the implanted phosphorus cannot penetrate into the deeper region of the former glass owing to the presence of heavy ^{89}Y. Consequently, the saturation amount of the phosphorus ion is smaller in the former glass than in the latter glass.

As shown in Fig. 2, the peak at 1150 cm^{-1} shifted to lower wavenumber by the P^+ ions implantation. This shift is attributed to the formation of structural damage, i.e. represented as a decrease in Si-O-Si bond angle between SiO_4 tetrahedra at the surface of the glass [9, 11]. This structural damage was also formed at the surface of P^+-implanted silica glass plates or microspheres as mentioned in the previous chapters.

The Y_2O_3-Al_2O_3-SiO_2 glass was colored brown by the phosphorus ion implantation. This coloration and the XPS spectra indicate that most of the phosphorus implanted into the Y_2O_3-Al_2O_3-SiO_2 glass exists in a form of the elemental phosphorus colloid, similar to that implanted into silica glass [12], for all the examined doses, although some of the phosphorus exists in a form of phosphorus oxide at the glass surface for doses of 5×10^{17} and 1×10^{18} cm^{-2} (See Fig. 3). The phosphorus oxide is considered to be formed near the surface because the phosphorus ions were distributed up to the surface for high doses of 5×10^{17} and 1×10^{18} cm^{-2} and oxidized by the atmospheric oxygen. For doses of 5×10^{16} and 1×10^{17} cm^{-2}, the phosphorus ions were not distributed so as to reach the surface and hence the phosphorus oxide was not formed at the glass surface. In the case of silica glass plates in Chapter 4, the phosphorus was not distributed up to the surface even with a high dose of 1×10^{18} cm^{-2}. This can be also explained by assuming that the phosphorus can not penetrate into deeper regions of Y_2O_3-Al_2O_3-SiO_2 glass owing to the presence of heavy ^{89}Y.

By the P^+ ion implantation with a dose of 1×10^{18} cm^{-2}, yttrium ions moved toward the glass surface (See Fig. 1) and then a small amount of some crystalline phase was formed at the glass surface (See Fig. 4). This crystalline phase may mainly contain yttrium, because a shoulder was newly observed on Y_{3d} XPS spectrum of P^+-implanted Y_2O_3-Al_2O_3-SiO_2 glass (See Fig. 5), whereas no obvious change was observed for Si_{2p} and Al_{2p} XPS spectra.

On the basis of these structural findings, the dependence of the release of the Si, P, Al and Y from the Y_2O_3-Al_2O_3-SiO_2 glass into the hot water on the dose of P^+ ion implantation, shown in Fig. 6, might be interpreted as follows. The Y_2O_3-Al_2O_3-SiO_2 glasses, implanted with P^+ ions with doses of 5×10^{16} and 1×10^{17} cm^{-2}, released little amount of Si, P, Al and Y into hot water. The little amount of phosphorus released from these glasses is attributed to the lack of the phosphorus at the surface of the glass (See Fig. 2 (a) and (b)). The release of silicon from these glasses was as little as that from the unimplanted Y_2O_3-Al_2O_3-SiO_2 glass (See Fig. 6). This indicates that the change in Si-O-Si bond angle in the Y_2O_3-Al_2O_3-SiO_2 glass, formed by the ion implantation, has no effect on the chemical durability of the Y_2O_3-Al_2O_3-SiO_2 glass. On the contrary, the Y_2O_3-Al_2O_3-SiO_2 glasses implanted with P^+ ions with doses above 5×10^{17} cm^{-2} released appreciable amounts of Si, P, Al and Y. For doses above 5×10^{17} cm^{-2}, the presence of the phosphorus oxide at the glass surface (See Fig. 2 (c) and (d)) might contribute to the appreciable release of these elements from the glass into hot water, since the phosphorus oxide is known to be hygroscopic [13]. It can be seen from the present results and previous results on silica glass in Chapters 1-4 that the phosphorus oxide at the glass surface give detrimental effect on the chemical durability of the Y_2O_3-Al_2O_3-SiO_2 glass, similar to silica glass.

Although the Y_2O_3-Al_2O_3-SiO_2 glass implanted with P^+ ions with doses of 5×10^{16} and 1×10^{17} cm^{-2} released little amount of phosphorus into

hot water (See Fig. 6), the intensity of the broad peak in RBS spectrum at 200-300 in channel number was decreased after the soaking (See Fig. 7). This indicates that silicon, phosphorus and/or aluminum released into water in some extent during the soaking. In fact, the amount of silicon released from Y_2O_3-Al_2O_3-SiO_2 glasses implanted with doses of 5×10^{16} and 1×10^{17} cm^{-2} (≈ 0.8-0.9 ppm) was larger compared with that from silica glass implanted with P^+ ions at 200 keV with doses of 5×10^{16} and 1×10^{17} cm^{-2} (≈ 0.1 ppm).

The number of the phosphorus ions present in a microsphere of 20 μm in diameter of Y_2O_3-Al_2O_3-SiO_2 glass implanted with P^+ ions with a dose of 1×10^{17} cm^{-2} is 2.10×10^{-12} mol. On the other hand, the number of yttrium ions present in one microsphere in the same size of the glass of the composition $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%), which is already clinically used for the radiotherapy, is 4.88×10^{-11} mol. Therefore, the number of phosphorus ions in one glass microsphere is about 5% of that of yttrium ions for a dose of 1×10^{17} cm^{-2}. Even with this dose, the radiotherapeutic effect of the Y_2O_3-Al_2O_3-SiO_2 glass could be enhanced, since a half-life of ^{32}P (14.3 days) is about five times as long as that of ^{90}Y (64.1 h).

In conclusion, it is believed that the radiotherapeutic effect of Y_2O_3-Al_2O_3-SiO_2 glass could be enhanced by P^+ ions implantation at 200 keV with a dose of 1×10^{17} cm^{-2} without losing its high chemical durability.

5. Summary

In this chapter, P^+ ion implantation was extended to the Y_2O_3-Al_2O_3-SiO_2 glass, which is already clinically used, in order to enhance its radiotherapeutic effect. The amount of the implanted phosphorus was saturated at a dose as low as 5×10^{17} cm^{-2} for this glass even under 200 keV. The phosphorus was distributed up to the glass surface and a part of it was oxidized at the surface for doses of 5×10^{17} cm^{-2}, whereas it was not present at the surface for doses below 1×10^{17} cm^{-2}. These properties characteristic to this glass is attributed to larger masses of the constituent elements. The glasses implanted with P^+ ions at doses below 1×10^{17} cm^{-2} hardly released any elements of the silicon, phosphorus, aluminum and yttrium into water at 95°C even after 7 days. For a dose of 1×10^{17} cm^{-2}, the number of the phosphorus ions in one Y_2O_3-Al_2O_3-SiO_2 glass microsphere 20 μm in diameter is only about 5% of that of yttrium ions. Even with this dose, the radiotherapeutic effect of the Y_2O_3-Al_2O_3-SiO_2 glass could be appreciably enhanced, since a half-life of ^{32}P (14.3 days) is about five times that of ^{90}Y (64.1 h).

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GENERAL SUMMARY

The present thesis has described the study on structure and chemical durability of P^+-implanted glasses for *in situ* radiotherapy of cancer. It was shown that P^+ ion implantation technique can give microspheres of SiO_2 and Y_2O_3-Al_2O_3-SiO_2 glasses containing large amount of the phosphorus without losing their high chemical durabilities, and thus obtained microspheres are believed to be useful for *in situ* radiotherapy of cancers. The contents of the respective chapters are summarized as follows:

In Chapter 1, P^+ ion implantation into silica glass plates was attempted at the acceleration energy of 20 keV with doses of 1×10^{16} to 2×10^{17} cm^{-2}. The amount of the phosphorus was saturated at a low dose of about 5×10^{16} cm^{-2} under 20 keV. Structural damage, represented as a decrease in Si-O-Si bond angle between SiO_4 tetrahedra, was formed at the glass surface by the ion implantation, independent of the ion dose. The implanted phosphorus formed elemental phosphorus in a form of colloids in the glass and a part of it near the surface was oxidized by the atmospheric oxygen. The silica glass plate implanted with P^+ ions at 20 keV released appreciable amounts of silicon and phosphorus into water at 95°C for 7 days even with a low dose of 1×10^{16} cm^{-2}. Such low chemical durability of the glass was attributed to the presence of oxidized phosphorus at the surface of the glass.

In Chapter 2, P^+ ion implantation into silica glass plates was carried out at the acceleration energy of 50 keV with doses of 5×10^{16} to 1×10^{18} cm^{-2}. Under this acceleration energy, the amount of the phosphorus in the glass was saturated at a dose of about 5×10^{17} cm^{-2}, which is higher than that under 20 keV. Structural damage in the Si-O-Si network was formed at the glass surface under 50 keV, similar to 20 keV. The implanted phosphorus was localized only in the regions deeper than 1.2 nm from the surface, taking a form of phosphorus colloids, for a dose of 5×10^{16} cm^{-2}, whereas it was distributed up to the glass surface and a part of it near the surface was oxidized for doses above 1×10^{17} cm^{-2}. The former glass little released both the silicon and phosphorus into water at 95°C even after 7 days, whereas the latter glasses released appreciable amounts of these elements. This indicates that the structural damage in the Si-O-Si network induced by the ion implantation gives no adverse effect on the high chemical durability of the silica glass, and that the implanted phosphorus gives no detrimental effect on the chemical durability of the silica glass, when it is localized in a deep region from the surface, but does give it, when it is distributed up to the surface to be oxidized. This indicates that a higher acceleration energy makes the phosphorus to be localized in a deeper region of the glass to give a chemically durable glass containing a larger amount of the phosphorus.

In Chapter 3, acceleration energy of P^+ ion implantation into silica glass plates was increased up to 100 keV. The amount of the phosphorus

in the glass was saturated at a dose of about 5×10^{17} cm^{-2}, similar to under 50 keV. Little phosphorus was present in the surface region, at least to a depth of 2.4 nm even for a high dose of 1×10^{17} cm^{-2}, whereas an appreciable amount of it was distributed up to the glass surface and a part of it was oxidized for doses above 5×10^{17} cm^{-2}. The glasses implanted with doses below 1×10^{17} cm^{-2} hardly released both of the phosphorus and silicon into water at 95°C even after 7 days, whereas the glasses implanted with doses above 5×10^{17} cm^{-2} released appreciable amounts of these elements. The number of the phosphorus ions present in the silica glass implanted with P^+ ions at a dose of 1×10^{17} cm^{-2} corresponds to only about 10% of the number of the yttrium ions in the $17Y_2O_3$-$19Al_2O_3$-$64SiO_2$ (mol%) glass for one microsphere 20 μm in diameter. Therefore, P^+ ion must be implanted at a higher energy in order to obtain a chemically durable silica glass containing the phosphorus in the amount comparable to the yttrium in the Y_2O_3-Al_2O_3-SiO_2 glass.

In Chapter 4, acceleration energy of P^+ ion implantation was furthermore elevated up to 200 keV, which is the highest energy available with the popular ion implanter commercialized. The amount of phosphorus in the glass was not saturated even at a high dose of 1×10^{18} cm^{-2} under this acceleration energy. Nearly all the implanted phosphorus was not present not at the surface but in the inner region of the glass, taking a form of phosphorus colloid for all the doses in the range from 5×10^{16} to 1×10^{18} cm^{-2}. It was observed that the implanted phosphorus formed

amorphous phosphorus colloid particles in diameters ranging from 10 to 150 nm, being distributed widely in a layer centered at 200-250 nm depth, in the silica glass implanted with a dose of 1×10^{18} cm^{-2}. The silica glass implanted even with a high dose such as 1×10^{18} cm^{-2} hardly released both of the phosphorus and silicon into water at 95°C for 7 days. This is in contrast with the results for implantation energies of 20, 50 and 100 keV, where even doses of 5×10^{16}, 1×10^{17} and 5×10^{17} cm^{-2}, respectively, gave the oxidized phosphorus on the glass surfaces and appreciable releases of the phosphorus and silicon into the hot water. This indicates that a chemically durable silica glass containing the phosphorus in the amount comparable to the yttrium in the Y_2O_3-Al_2O_3-SiO_2 glass can be obtained, when P^+ ion is implanted at a high energy to be localized in a deep region from the glass surface without forming chemically less durable oxidized phosphorus at the glass surface, even if the surface structure is damaged by the ion implantation.

In Chapter 5, P^+ ion implantation was attempted to apply to silica glass microspheres 20 to 30 μm in diameter, which can be used for practical *in situ* radiotherapy. The phosphorus ion was implanted to the microspheres vibrating in a bucket with nominal doses of 2.5×10^{16} and 3.35×10^{16} cm^{-2} at 50 keV. It was confirmed that the phosphorus ion can be uniformly implanted to the individual microspheres by this method. The implanted phosphorus was localized in deep region of the glass microsphere with the maximum concentration at about 50 nm in depth

without distributing up to the surface even for a nominal dose of 3.35×10^{16} cm^{-2}. Both the samples little released both the phosphorus and silicon into water at 95°C for 7 days. In view of the results on P^+ ion implantation to the silica glass plates, it is expected that silica glass microspheres containing more phosphorus which is desired for actual treatment could be obtained without losing its high chemical durability, if P^+ ion would be implanted at a higher energy with higher doses by the present method.

In Chapter 6, P^+ ion implantation was extended to the Y_2O_3-Al_2O_3-SiO_2 glass, which is already clinically used, in order to enhance its radiotherapeutic effect. The amount of the implanted phosphorus was saturated at a dose as low as 5×10^{17} cm^{-2} for this glass even under 200 keV. The phosphorus was distributed up to the glass surface and a part of it was oxidized at the surface for doses of 5×10^{17} cm^{-2}, whereas it was not present at the surface for doses below 1×10^{17} cm^{-2}. These properties characteristic to this glass is attributed to larger masses of the constituent elements. The glasses implanted with P^+ ions at doses below 1×10^{17} cm^{-2} hardly released any elements of the silicon, phosphorus, aluminum and yttrium into water at 95°C even after 7 days. For a dose of 1×10^{17} cm^{-2}, the number of the phosphorus ions in one Y_2O_3-Al_2O_3-SiO_2 glass microsphere 20 μm in diameter is only about 5% of that of yttrium ions. Even with this dose, the radiotherapeutic effect of the Y_2O_3-Al_2O_3-SiO_2 glass could be appreciably enhanced, since a half-life of ^{32}P (14.3 days) is about five times that of ^{90}Y (64.1 h).

On the basis of the results described above, it can be concluded that chemically durable glass microspheres containing a large amount of phosphorus, which are useful for *in situ* radiotherapy, could be obtained if P^+ ion is implanted at a energy as high as 200 keV.

LIST OF PUBLICATIONS

The studies in this thesis were published or are to be published on the following articles.

CHAPTER 1

"Preparation of Glasses for Radiotherapy by Ion Implantation,"

M. Kawashita, T. Yao, F. Miyaji, T. Kokubo, G. H. Takaoka and I. Yamada, *Radiat. Phys. Chem.*, **46**, 269-274 (1995).

CHAPTER 2

"Properties of Silica Glass Implanted with Phosphorus Ion at 50 keV for Radiotherapy,"

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CHAPTER 3

"Preparation of Radiotherapy Glass by Phosphorus Ion Implantation at 100 keV,"

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CHAPTER 4

"Phosphorus-Implanted Glass for Radiotherapy: Effect of Implantation Energy,"

M. Kawashita, F. Miyaji, T. Kokubo, G. H. Takaoka, I. Yamada, Y. Suzuki and K. Kajiyama, *J. Am. Ceram. Soc.*, submitted.

CHAPTER 5

"Preparation of Phosphorus-Containing Silica Glass Microspheres for Radiotherapy of Cancer,"

M. Kawashita, F, Miyaji, T. Kokubo, G. H. Takaoka, I. Yamada, Y. Suzuki and K. Kajiyama, *J. Biomed. Mater. Res.*, submitted.

"P^+-Implanted Silica Glass Microspheres for Radiotherapy of Cancer,"

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CHAPTER 6

"Structure and Properties of P^+-Implanted Y_2O_3-Al_2O_3-SiO_2 Glass for Radiotherapy of Cancer,"

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